SYNTHETIC AND STRUCTURAL STUDIES ON THE 1,3-DIPHENYLCYCLOBUTENYL CATION THE PROBLEM OF 1,3-ORBITAL OVERLAP

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ABDOLJALIL MOSTASHARI
1969

This is to certify that the

thesis entitled

SYNTHETIC AND STRUCTURAL STUDIES ON THE 1,3-DIPHENYL-
CYCLOBUTENYL CATION THE PROBLEM OF 1,3-ORBITAL OVERLAP

presented by

Abdoljalil Mostashari

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Organic Chemistry

Donald G Farnum
Major professor

Date December , 1969

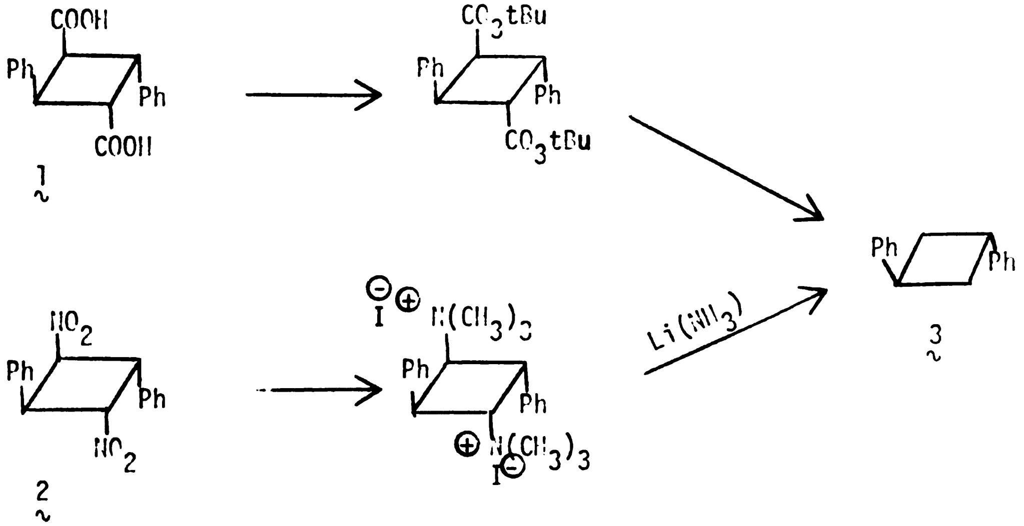
ABSTRACT

SYNTHETIC AND STRUCTURAL STUDIES ON THE 1,3-DIPHENYLCYCLOBUTENYL CATION. THE PROBLEM OF 1,3-ORBITAL OVERLAP.

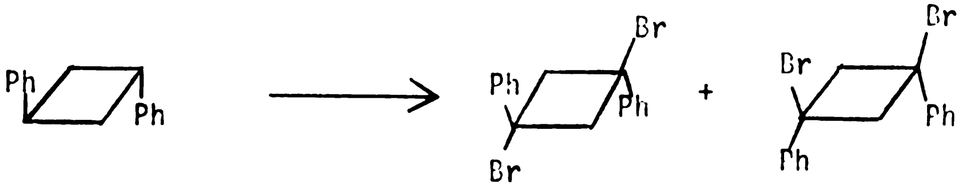
By

Abdoljalil Mostashari

In order to examine the possibility of 1,3-orbital overlap in the cyclobutenyl cation system[1], the *para*-proton chemical shift[2] of the 1,3-diphenylcyclobutenyl cation was determined. This cation was synthesized from available precursors: α-truxillic acid **1** and β-nitrostyrene dimer **2** were converted to *trans*-1,3-diphenylcyclobutane **3**.

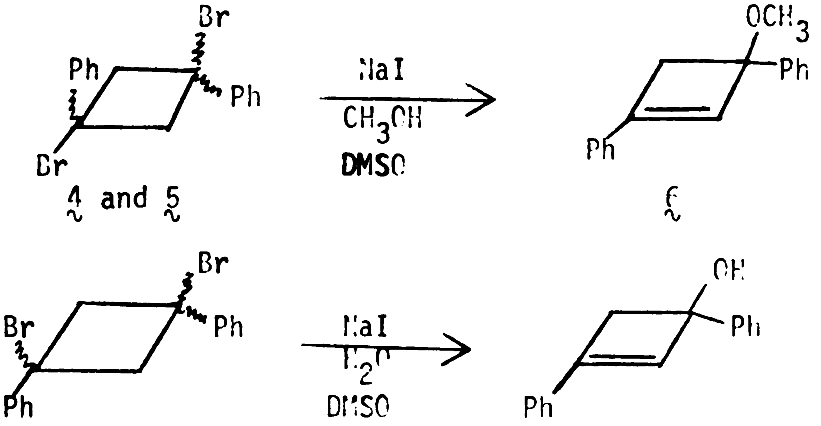


The hydrocarbon **3** was dibrominated to both possible isomers **4** and **5**.



4 5

Both of the dibromo derivatives were converted in good yields to the corresponding cyclobutenyl derivatives, 6 and 7, by a novel method which used sodium iodide as displacement catalyst in dimethyl sulfoxide as solvent.

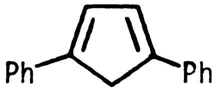


4 and 5

6

7

In order to interpret the results, the 1,3-diphenylcyclopentenyl and 1,3-diphenylcyclohexenyl cations were prepared as model compounds from their corresponding dienes: 8[3] and 9[4].



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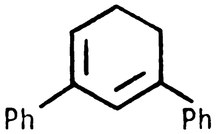

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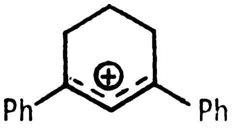
The *para*-protons of the three cations 10, 11 and 12 appeared at τ 2.14, 2.10 and 1.98 respectively in their nmr spectra.



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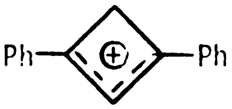

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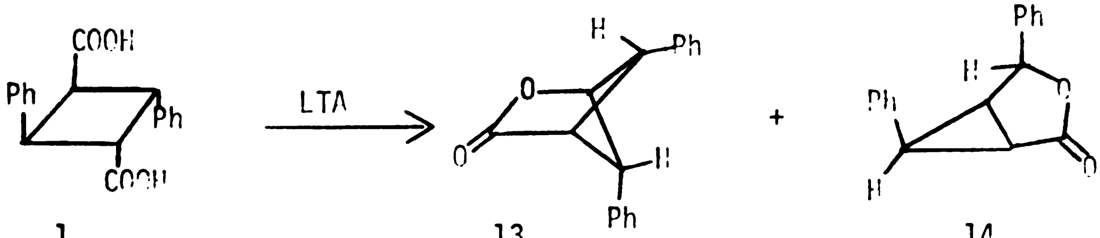
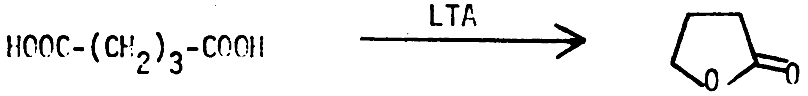
The increase of participation of the phenyl groups in stabilization of the cations from cyclohexenyl 10 to cyclobutenyl 12 was taken as evidence against predominance of 1,3-orbital overlap contribution in the stabilization of the latter ion. Instead, an electrostatic charge repulsion between positive charges on C_1 and C_3, which increases with the decrease in the distance between C_1 and C_3, was suggested to be responsible for the trend in the deshielding of the *para*-protons.

As an ancillary synthesis, the reaction of 1,3-dicarboxylic acids with lead tetraacetate was studied. γ-Lactones were found to be the only products. α-Truxillic acid 1 yielded two lactones 13 and 14.

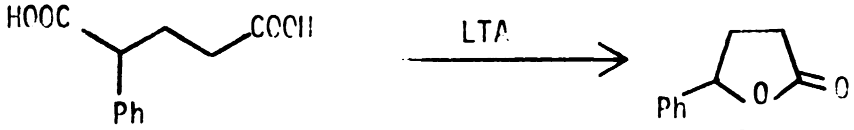


1 13 14

The reaction was found to be applicable to the available 1,3-diacids 15 and 17 which yielded γ-lactones 16 and 19 respectively.



15 16



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1969

To Enci
without whose love
this work would
not have been possible

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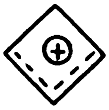
INTRODUCTION

The possibility of 1,3-π overlap in cyclobutenyl cation has been explored by Kiefer and Roberts[1]. They suggest that simple MO calculations predict a delocalization energy of 4.1-10.9 kcal/mole, when the 1,3 resonance integrals (β 1,3) are assigned values of 0.2-0.5 β based on the distance between C_1 and C_3. Their results imply that the structure of the cation could be better presented as (II) rather than (I).

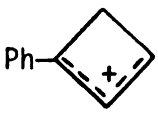


I

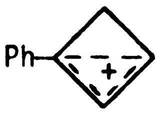
II

Based on this prediction, they investigated the solvolysis of 1-methylcyclobut-2-enyl bromide. They found that the relative rate of this compound compared with that of an open chain allylic model compound (α, γ, γ, trimethylallylbromide) was 1/17,000. The authors suggested that in the absence of 1,3-π overlap, this ratio should have been much smaller in view of the tremendous strain introduced in the already strained cyclobutene system in the transition state by addition of one more sp^2 center in the molecule. Based on corrective factors the authors introduce, they attribute an accelerating factor of 10^3-10^5 (corresponding to 4.7-7.0 kcal/mole) in the rate of solvolysis of the cyclobutenyl bromide.

In another investigation[2] acid catalyzed solvolysis of the p-nitrobenzoate of 3-phenyl-2-cyclobutenol was found to be only 7.8 times slower (corresponding to 1.1 kcal/mole) than that of methylcinnamyl alcohol p-nitrobenzoate. This type of solvolysis (A_{AL} I) which goes through a carbonium ion type transition state in a cyclobutene system should result in a difference of at least 5 kcal/mole of E_a rather than 1.1 kcal/mole. Roberts and coworkers therefore suggested that this difference is due to 1,3-π overlap in the intermediate cation as in cation (IV) which is presumably much more stable than III.

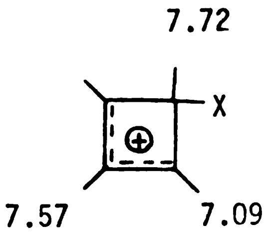


III



IV

Katz[3] has also interpreted the nmr spectra of some polymethyl cyclobutenium cations as supporting 1,3-π overlap. When he treated different 1,2,3,4-tetramethyl-3,4-dihalocyclobutenes with excess silver hexafluoroantimonate in methylene chloride, he only isolated one equivalent of silver halide and the nmr spectrum of the cation formed showed for instance for the dichloro compound: three signals at τ 7.09, 7.57 and 7.72 with relative intensities 2:1:1 assigned as follows. Based on



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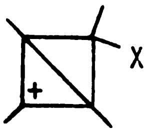


VI

a comparison with polymethylated cyclopentenyl cations he concluded that the allylic methyls at τ 7.09 were shifted upfield, while the central methyl at τ 7.57 was shifted downfield. He took this as evidence for a contribution from bicyclobutyl cation VI. However, we believe Katz has ignored some important effects on the chemical shifts. Thus, the hybridization in the strained cyclobutenyl cation will be different from that in the less strained cyclopentenyl cation. This will have an indeterminate effect on the directly attached methyls. Also, since the geometry is different in the two cations, the anisotropic effect of the allyl system on the attached methyls will be different - most probably resulting in an upfield shift of the allylic methyls on the cyclobutenyl cation. Therefore, we have some reservations about the reliability of Katz's conclusion of 1,3-overlap in the cyclobutenyl cation.

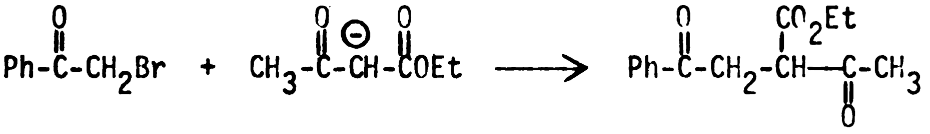
The studies reported in this thesis were undertaken in order to determine the possibility of the use of the para proton downfield shift in the nmr spectrum of 1,3-diphenyl substituted cyclobutenyl system as a measure of 1,3-π overlap. This criterion has been explored by D. G. Farnum[4]. It was reasoned that if there is any 1,3-π overlap as a major contributor to stability, then the para protons of the phenyls would feel less positive charge. Therefore, by comparison of their chemical shift with those of model compounds such as the 1,3-diphenylcyclohexenyl and 1,3-diphenylcyclopentenyl cations, the extent of the effect of 1,3-π interaction could be determined. It should be noted that from the approximate chemical shift-delocalization energy relationship suggested by Farnum[4], the delocalization energy of 4.1-10.9 kcal/mole expected from Roberts calculations[1] should be detectable by this method.

As a corollary part of these studies it was necessary to explore the synthesis of a number of small ring compounds as potential precursors to the 1,3-diphenylcyclobutenyl cation.

RESULTS AND DISCUSSION

I. *1,3-Diphenylcyclopentenyl System.* - A natural precursor of 1,3 diphenylcyclopentenyl cation was thought to be 1,3-diphenylcyclopent-2-ene-1-ol or the dehydrated analogue 1,3-diphenyl-1,3-cyclopentadiene. A literature survey showed no reported synthesis of the former, but the latter had been reported by Borsche and Menz[5], through a low yield preparation of 3-phenylcyclopent-2-en-1-one 1 and subsequent treatment of this ketone with phenyl magnesium bromide.

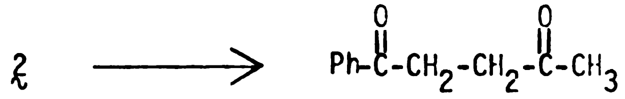
a) Preparation of 3-phenylcyclopent-2-ene-1-one (1). In this preparation the method of Borsche was employed. Condensation of the sodium salt of ethylacetoacetate with phenacyl bromide afforded the substituted acetoacetate ester 2. Saponification and decarboxylation



$$\mathrm{Ph-\overset{O}{\overset{\|}{C}}-CH_2Br + CH_3-\overset{O}{\overset{\|}{C}}-\overset{\ominus}{C}H-\overset{O}{\overset{\|}{C}}OEt \longrightarrow Ph-\overset{O}{\overset{\|}{C}}-CH_2-\overset{CO_2Et}{\overset{|}{C}H}-\underset{O}{\underset{\|}{C}}-CH_3}$$

2

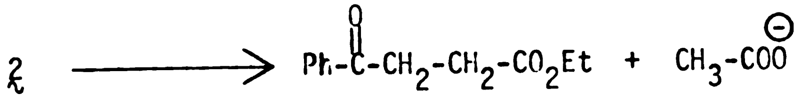
of 2 was carried out cccording to the modification of Wilds and Johnson[6], using very dilute aqueous potassium hydroxide (0.8%).



$$2 \longrightarrow \mathrm{Ph-\overset{O}{\overset{\|}{C}}-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-CH_3}$$

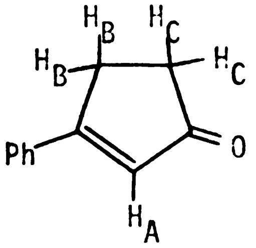
3

Use of a more concentrated solution of base leads to the undesired cleavage reaction:



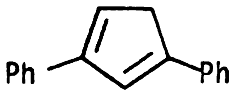
$$2 \longrightarrow \mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}CH_2{-}CO_2Et} + \mathrm{CH_3{-}COO^{\ominus}}$$

The diketone 3 was characterized by its spectroscopic properties. The two carbonyl stretching vibrations at 1720 and 1694 cm^{-1} are as expected for a simple aliphatic ketone and a benzoyl group respectively. The nmr spectrum shows a benzoyl pattern at τ 2.2 and 2.68 with relatively intensities of 2:3, the two methylene groups show an A_2B_2 pattern centered at τ 7.18 and the methyl ketone at τ 7.95. Ring closure was accomplished by treating diketone 3 with 10% KOH. The product 1 shows a doublet at 1705 (shoulder) and 1695 cm^{-1} in its ir spectrum which is apparently normal with cyclopentenones due to fermi resonance[7]. The nmr spectrum of 1 exhibits a 5 proton multiplet signal at τ 2.6 due to the phenyl group. The vinylic proton (H_A) is represented by a peak at τ 3.6 as a triplet J_{AB} = 1.5 cps. The A_2B_2 pattern centered at 8.35 is assigned to the two methylene groups, the lower field portion of the A_2B_2 at τ 8.05 (H_B) is more complicated by further coupling to H_A.



1

b) <u>Preparation of supposedly 1,3-diphenyl-1,3-cyclopentadiene</u>. The cyclopentadiene was prepared by treatment of the cyclopentenone 1 with phenyl magnesium bromide. The nmr spectrum of the cyclopentadiene product showed, besides the phenyl absorption, two triplets at τ 3.12 and 6.27 with relative intensities of 1:1. The two triplets with a coupling constant of 1 cps suggest a more symmetrical structure than 1,3 diphenyl-1,3-cyclopentadiene 4 which should show two vinyl hydrogens with different coupling constants with the methylene group. The spectrum rather suggests a structure of the type 5 or 6.



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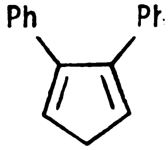

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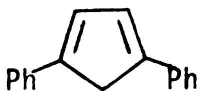

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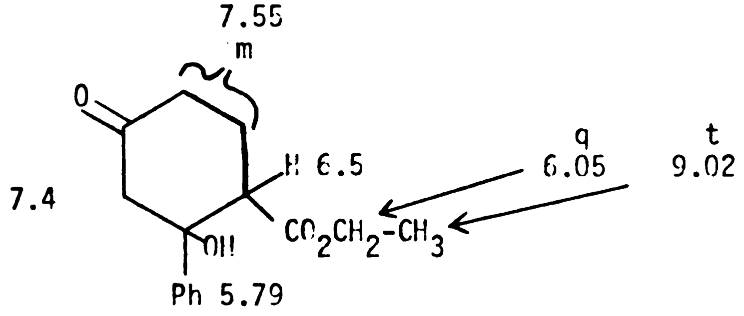
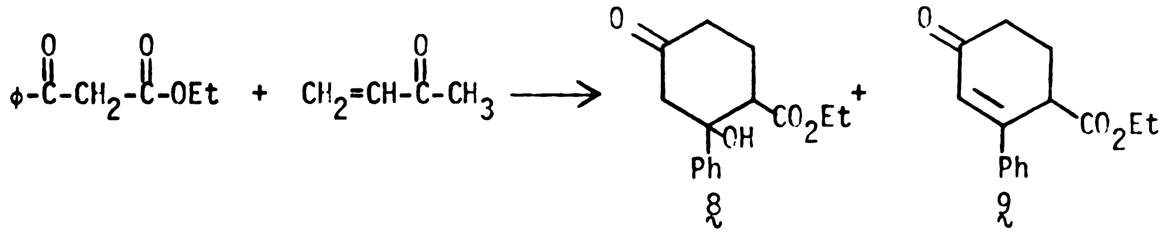
Structure 5 seems unlikely considering the synthetic route and small coupling constant involved. Structure 6 seemed to be best in accord with the nmr. A literature survey revealed that Drake and Adams[8] have reported a one step synthesis of 1,4-diphenyl-1,3-cyclopentadiene whose properties are identical with those of the described 1,3-diphenyl-1,3-cyclopentadiene. This compound later has been reported[9] to form Diels-Alder adducts of the 1,4-diphenyl substituted bicyclo[2.2.1]hexan structure.

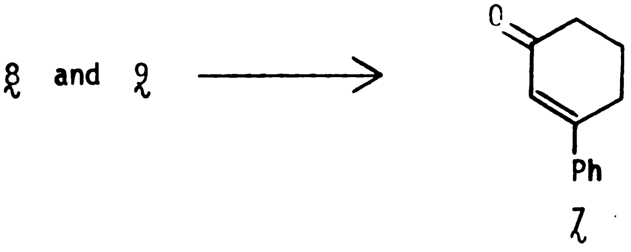
II. Preparation of 1,3-diphenyl-1,3-cyclohexadiene (10). - The title compound was prepared from treatment of 3-phenylcyclohex-2-ene-1-one 7 with phenyl magnesium bromide. Ketone 7 was in turn prepared by Walker's method[10]. Treatment of ethylbenzoylacetate with methylvinylketone in the presence of benzyltrimethylammonium hydroxide (triton B) as base yielded a mixture which was triturated with ether to give a solid. Walker failed to assign a structure to this solid but found the molecular formula to be $C_{15}H_{18}O_4$. The ir spectrum of this compound was also reported by him to exhibit absorptions at 3448 cm^{-1}, 1694 cm^{-1} and 1709 cm^{-1}. The nmr spectrum of this compound was found to be more helpful in structure elucidation. It shows a five proton multiplet at τ 2.72, a one proton broad singlet at τ 5.79, a two proton quartet at τ 6.05, a one proton multiplet at τ 6.5, a two proton singlet at τ 7.4, a four proton multiplet at τ 7.55 and a three proton triplet at τ 9.02 which were assigned to structure 8 as follows:



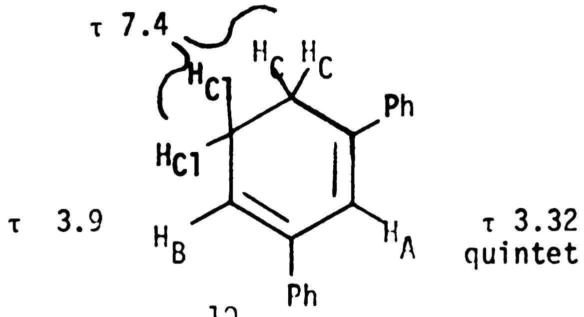
8 (τ values)

Assignment of the signal at 5.79 to the -OH proton was based on the fact that when the sample was shaken with D_2O, this signal disappeared. The keto ester 8 and the oil obtained from evaporation of the ethereal solution, to which Walker has assigned the structure 9, were both converted to ketone 7 on treatment with 10% KOH.





Ketone 7 shows a carbonyl stretching absorption at 1675 cm^{-1}. This ketone has been reported by several other investigators[11,12,13]. 1,3-Diphenylcyclohexadiene (10) was prepared by treatment of ketone 7 with phenylmagnesium bromide[11].



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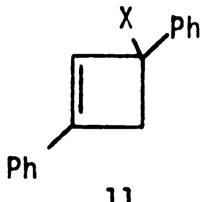
J_{AB} = 1 cps
J_{AC} = 0.5 cps
J_{BC_1} = 4.5 cps

Assignment of the low field vinylic absorption to H_A is based on the expected anisotropic effect of the two neighboring phenyl rings and the coupling constants.

III. *Preparation of diphenylcyclobutenyl cation precursor.* - Preparation of the potential precursors of 1,3-diphenylcyclobutenyl cation with the general structure 11 could have been persued via two routes.

a) Preparation of 1,3-diphenylcyclobutene (12) and function - alization of C_3 by halogenation at benzylic and allylic C_3;



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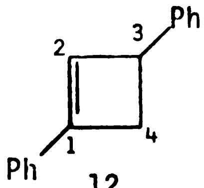
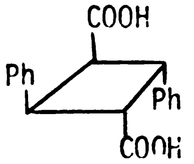


12

There are two reported syntheses of 12 in the literature[14,15], neither of which is on a preparative scale. The spectroscopic properties reported by the two authors are not in agreement. Furthermore 12 has been reported to be very unstable and decomposes rapidly[15]. Based on these difficulties this route was not pursued.

b) Preparation of 1,3-diphenyl cyclobutane 13 and conversion of this compound to the precursor 11, such as to avoid the intermediate cyclobutene 12. Although simple 1,3-diphenylcyclobutane has not been reported in the literature, substituted derivatives are very well known. Systems such as truxillic acid[16] (14), 1,3-diphenyl-2,4-dinitrocyclobutane (15) and 1,3-diphenyl-2,4-diacetylcyclobutane[18] (16) have been reported to be photodimers of β substituted styrenes.



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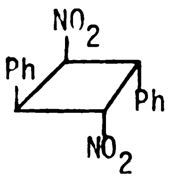

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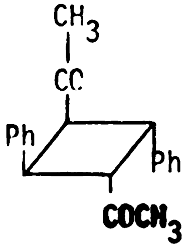

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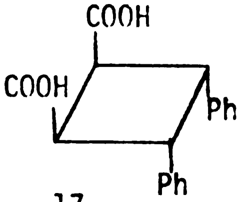
Ready availability of these compounds and available synthetic methods for decarboxylation of the acid or removal of the nitro group led us to believe that these compounds would be useful as synthetic intermediates in the preparation of 1,3-diphenylcyclobutane (13).

1-Photodimerization of *trans* cinnamic acid and β-nitrostyrene.

General: Solid state photodimerization of *trans* cinnamic acid has been studied extensively and most of the possible isomers of the dimer have been isolated[19]. Practically, however, solid state photolysis of *trans* cinnamic acid could only be carried out with small amounts. Stirring of a solid which would allow all the crystals to be exposed to light is a problem in irradiation of large amounts. Suspension of the crystals in water on the other hand had been reported to proceed in low yields (2.5-9.5%)[20,21] over long periods of time. The problem was thought to be that the crystals are not fully exposed to light. When the source of light was placed inside a suspension of commercial cinnamic acid in water and the suspension was stirred vigorously a good yield (20-60%) of dimer was obtained. Commercial cinnamic acid, which is presumably deposited quickly at the time of preparation, has been reported to give only the undesired isomer β-truxinic acid[22] (17) when irradiated in the solid state.



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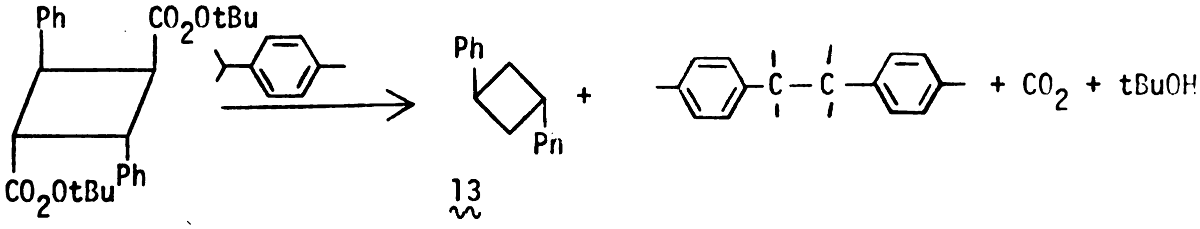
However, in our study, α-truxillic acid (14) seemed to be the only product. This is perhaps due to the solution of the metastable β form of trans cinnamic acid in water and recrystallization as the stable α form. This oonversion has elegantly been demonstrated by Cohen and Schmidt[23].

Preparation of trans-1,3-diphenylcyclobutane (13).

Decarboxylation of simple secondary carboxylic acids doesn't seem to be an easy task. Conventional methods such as quinoline and copper or basic or acidic decarboxylations are applicable only in the case of unsaturated acids or β keto acids and so on. Wiberg[24] et al had reported decarboxylation of bicyclo[2.1.1]hexane-5-carboxylic acid by conversion of the acid to the t-butylperester and subsequent decomposition of the perester in p-cymene. This method has been successfully used by Eaton[25] in the conversion of cubane dicarboxylic acid to the parent hydrocarbon in moderate yield.

Although Eaton has applied this reaction to cubane dicarboxylic acid, it was suspected that our case would be much more like the reaction of vicinal diacids in which the carbon radicals could combine[26]. Therefore, we expected complications from this method. The diperester of truxillic acid, 18, was prepared by the reaction of the bis acid chloride with t-butyl hydroperoxide. The perester, a seemingly stable solid, which was titrated to be 94-95 percent active, showed a carbonyl stretching vibration at 1745 cm^{-1} which has been reported for other peresters[27]. When the diperester was heated in p-cymene or p-diisopropylbenzene, it decomposed to give trans-1,3-diphenylcyclobutane(13) in moderate yield. Isolation of the desired product from the product mixture proved to be difficult. Extensive column chromatography was necessary to separate 13 from the dimers of the solvents. The most convenient method of separation was found to be preparative vapor phase chromatography which is accompanied by approximately 30% loss, but yields pure hydrocarbon.



The nmr spectrum of 13 shows a quintet at τ 6.4 and a triplet at τ 7.48 J = 6.8 cps with relative intensities of 1:2. The signal at lower field was assigned to the benzylic protons coupled to four α protons, and the triplet was assigned to the two methylene groups.

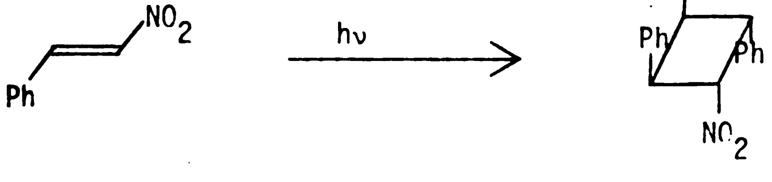
An alternative synthesis of 1,3-diphenylcyclobutane (13).

The difficulty in isolation of cyclobutane in the diperester decomposition method made us look for an alternative synthesis of 1,3-diphenyl cyclobutane. Photodimerization of β-nitro styrene has been reported to proceed in moderately good yield to trans, trans, trans-1,3-diphenyl-2,4-dinitrocyclobutane[28] (15). This compound could be reduced to the corresponding diamine which could be deaminated by one of several methods reported for reductive deamination of aliphatic amines. Nickon[29] treated amine sulfonamides with hydroxyl amine-O-sulfonic acid in alkaline solution:

$$R\text{-}NH\text{-}SO_2Ar \xrightarrow[OH^{\ominus}]{NH_2X} ArSO_2^{\ominus} + N_2 + R\text{-}H$$

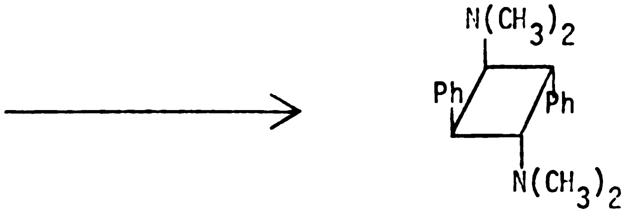
$$X = OSO_3H \text{ or } Cl$$

This method, however, is tedious and the yields are usually low to moderate. Another method reported by Grovenstein and Rogers[30] at the same time is much simpler and deals with cleavage of quarternary ammonium salt with sodium in liquid ammonia. Reduction of dinitro compound 14 to the diamino analog and conversion of the amine to the quarternary ammonium salt should not be difficult. Therefore an alternate route to the cyclobutane 13 was devised as shown below:



14

14



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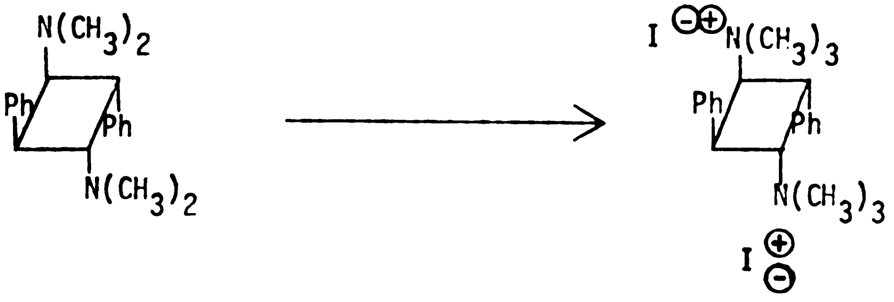

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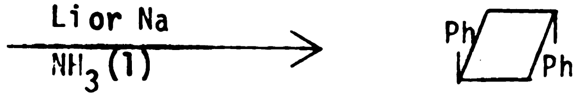
16



13

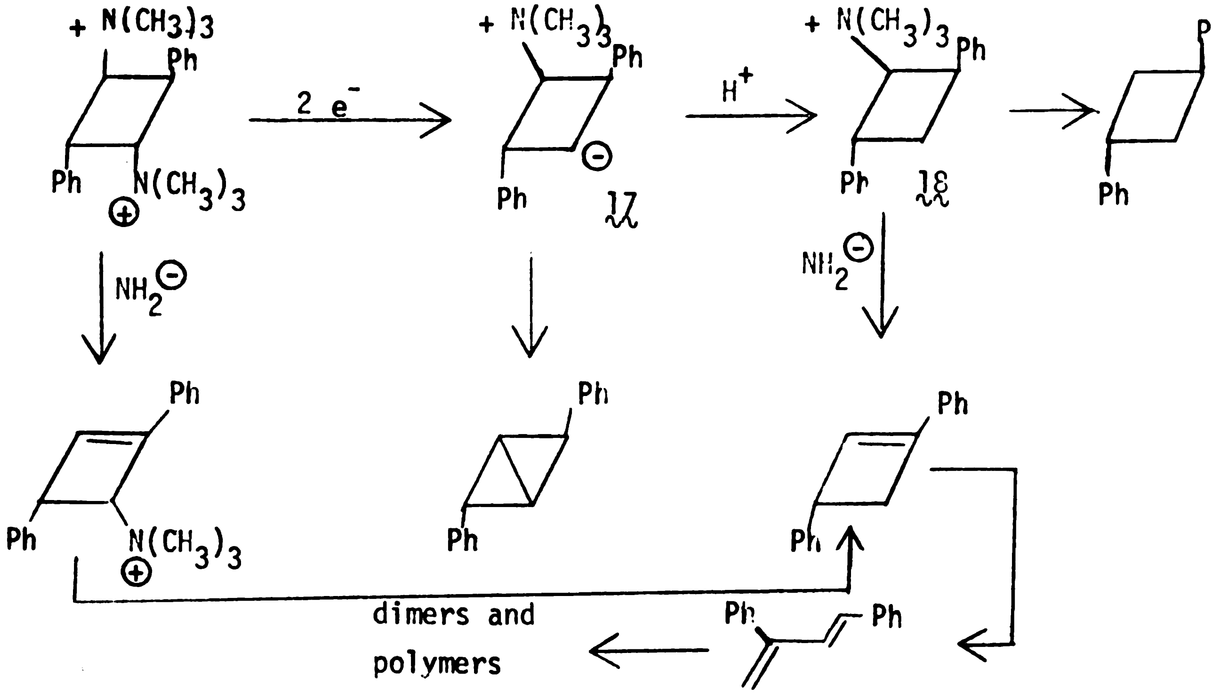
Photodimerization of β-nitrostyrene. The apparatus used for this reaction was very simple: an 18 inch crystallization dish and a 550 W Hanovia lamp jacketed by a Pyrex cooling well. The suspension method gave very good yields of the dimer 14. The dimerization had been reported in the solid state to give yields of 25-40% over a period of three weeks[28]. The suspension method gave yields of 35-50% within 24 hrs. When the crystallization dish was cooled to 18-20° in a water bath the dimerization yield increased to 50-70% in a 24 hrs period of irradiation. Separation of dimer was accomplished by soxhlet extraction of the mixture of dimer and monomer. This gave almost pure dimer which was further purified by recrystallization from benzene. The nmr of 14 shows an AA'BB' system centered at τ 6.6 with $\nu_B - \nu_A$ = 53 cps at 60 Mc.

Reduction and alkylation of dinitrodiphenylcyclobutane (14)

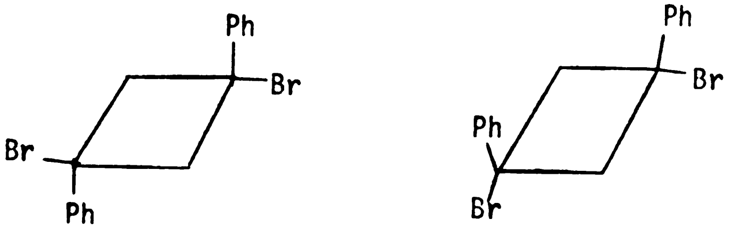
Reduction by zinc and hydrochloric acid of 14 has been reported[28]. No yield has been reported for this reaction since the resultant diamine was too unstable to be isolated. On the other hand, this amine has been obtained by Curtius degradation of α-truxillic acid[21], and subsequently converted to the bis(dimethyl) analog 15 in 66% yield[31] by using the Eschweiler-Clarke[32] modification of the Leuckart reaction, which consists of reductive amination of formaldehyde by formic acid. It occurred to us that combination of the reduction of the dinitro compound 14 and alkylation of the diamine therefrom with formaldehyde and formic acid is possible by using formic acid both as an acid in combination with the zinc and as reducing agent for conversion of imines obtained from the reaction of formaldehyde with the produced amine. Thus when the dinitro compound 14 was treated with a large amount of formic acid and zinc dust in the presence of formaldehyde, a good yield (50-80%) of 1,3-diphenyl-2,4-bis-(dimethylamino)cyclobutane (15) was obtained which in most cases didn't need purification. The reaction of zinc dust and formic acid is very vigorous and formic acid has to be added dropwise with initial heating to start the reaction. In one instance there was seemingly no reaction until all of the acid had been added. Then, 5-10 minutes after the addition was finished, a vigorous reaction took place which can be called an explosion. The purity and yield of 15 was proportional to the amount of zinc dust and especially of formic acid For an 80 g run of 14, 600-800 ml of formic acid is necessary for the best results. The impurities are usually monomethyl, bis(monomethyl), and 2-dimethylamino-4-monomethylamino compounds. In cases when purification was found necessary the best method was found to be chromatography of the mixture on alumina rather than sublimation as previously reported[31]. 15 is eluted with hexane and crystallizes as it comes out of the column. It could be used without further purification (mp 119-122°). One recrystallization from hexane gives pure 15. Attempted reductive alkylation of dinitro compound 14 by hydrogenation in the presence of formaldehyde failed[33], and only with Raney Nickel catalyst a yield of 1% of 15 was obtained. 15 shows an interesting doublet at 2800 cm^{-1} and 2850 cm^{-1} which is due to C-H stretching of methyl groups attached to nitrogen[34].

Preparation of bis-(methiodide)(16) White and Dunathan prepared this compound from the reaction of 15 with excess methyl iodide in methanol for 7 days in 77% yield . It was found that reaction goes much faster and cleaner in dry acetone with initial brief heating on a steam bath to give an 85-90% yield in 20-30 minutes. The methiodide obtained has a much higher melting point and recrystallization is not necessary.

Reductive Deamination. Cleavage of bis-(methiodide) 16 was accomplished by lithium in liquid ammonia with isopropanol as a proton source[35]. A mixture of 1,3-diphenylcyclobutane (14) and some other hydrocarbons was obtained in which 14 is recognized by its characteristic peaks in the nmr spectrum of the mixture. The total yield of hydrocarbon is 50-55%. Isolation of 14 by conventional methods was not possible and the mixture was successfully used in subsequent syntheses as a source of cyclobutane 14. The hydrocarbon impurities are perhaps the product of side reactions of intermediates 17 and 18 such as those illustrated.



Preparation of 1,3-dibromo-1,3-diphenylcyclobutane (19). In order to avoid preparation of the unstable 1,3-diphenylcyclobutene, it was decided to convert cyclobutane 14 to dibromide 19, and then either selectively dehydrohalogenate one of the bromines, or alternatively substitute one of the bromines with another functional group (such as methoxide) and then dehydrohalogenate the other bromine. Dibromination of pure 14 yielded two different isomers. Analysis of both indicated $C_{16}H_{14}Br_2$ and both behaved similarly in subsequent reactions. The isomer (a) mp 145-145.5° was first to crystallize out of an ether solution of the mixture in the form of needles. It shows a simple nmr pattern: a ten proton multiplet at τ 2.6 and a four proton singlet at τ 5.85. The other isomer (b) could not be obtained pure but was always contaminated with a bit of the isomer (a) and was analyzed as such. It shows the same pattern in the nmr, only the phenyl multiplet is shown at τ 2.7 and the methylene protons at τ 6.0. Since the bromo compounds are decomposed on heating and because subsequent reactions showed that both react to give the same product in different reactions, no further attempts at the separation were made and the products were assumed to have structures 19a and 19b.



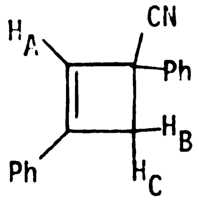
19 (a and b)

The nmr is unexpected because it suggests that both of the protons of the methylene groups in both isomers are magnetically equivalent. It could only be said that the chemical shifts are fortuitously the same. Both isomers are unstable and decompose in air and on being heated in solution.

Attempts at conversion of dibromocyclobutane 19 to cyclobutenyl derivatives. Selective substitution or dehydrohalogenation of one of the bromines in 19a or the mixture of 19a and 19b was unsuccessfully tried by reacting them with sodium methoxide in methanol, sodium methoxide in THF, sodium bicarbonate in THF, lithium chloride in DMF, sodium iodide in THF, sodium iodide in methanol or potassium carbonate in DMSO. In all cases the disubstituted compound or starting material or intractable polymeric material was obtained.

Preparation of 1,3-diphenylcyclobut-2-enylcyanide (20). In a review of the attempted reactions it was decided that all of the reagent used are either strong bases and poor nucleophiles or weak bases.

Consequently they are either unable to effect a reaction or they dehydrohalogenate both of the bromines or displace both of them. It seemed necessary to find a reagent which is a good nucleophile and a moderate base. Sodium cyanide is a good nucleophile but in aqueous solvent it is a strong base due to hydrolysis, on the other hand, it does not dissolve or ionize in most organic solvents. Dimethyl sulfoxide seemed to be the solvent of choice since it has a high ionization power and it was found that it also dissolves sodium cyanide. Reaction of the dibromide **19a** or the mixture of **19a** and **19b** with sodium cyanide in dimethyl sulfoxide gave an 80-90% yield of the title compound (**20**) which was easily purified by chromatography over Florisil. **20** is eluted with hexane as a yellow oil. Its ir spectrum shows a band at 2220 cm^{-1} characteristic of cyanides (-C≡N), and its nmr shows a ten proton signal at τ 2.70 as a multiplet, a sharp one proton singlet assigned to H_A at τ 3.72 and an AB quartet worth two protons centered at 6.79, J_{AB} = 13 cps assigned to H_C and H_B.

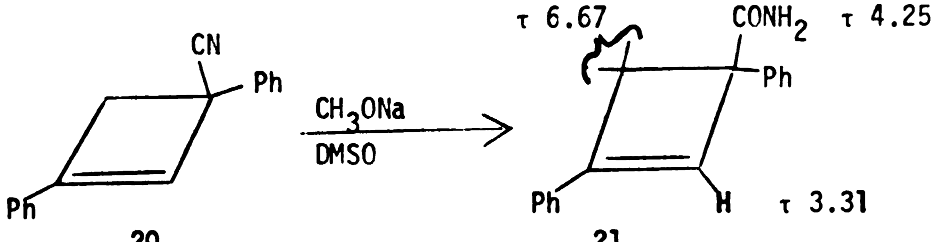


20

Attempted conversion of the cyanide **20** to the corresponding amide or acid. Hydrolysis of cyanide **20** by alkaline hydrogen peroxide[36] at room temperature was unsuccessful and a mixture of starting material and intractable material was obtained. A reported method for hydrolysis of nitriles with manganese dioxide in methylene chloride[37] at room temperature for 60 hrs failed to convert the cyanide into the corresponding amide, but resulted in substantial decomposition to intractable materials. Basic hydrolysis with sodium hydroxide or acidic hydrolysis with hydrobromic acid were found unsuccessful.

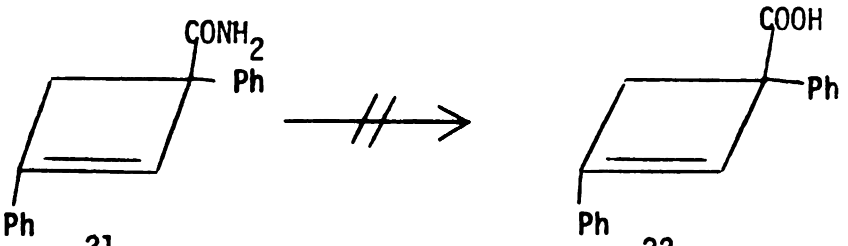
Preparation of 1,3-diphenylcyclobut-2-ene carboxamide (**21**).

A literature survey showed that at least in one case a quarternary nitrile had been converted to the corresponding imido-ester when treated with sodium ethoxide[38]. The method was used to convert the cyanide **20** to amide **21**. The cyanide **20** was added to a solution of sodium methoxide in dimethylsulfoxide. After 48 hrs, aqueous workup and extraction with ether gave the amide **21** in good yield as a solid: mp 143-145°; carbonyl absorption at 1685 cm^{-1} is characteristic of amides. This is substantiated by a doublet at 3360 and 3500 cm^{-1}. The nmr spectrum of **21** is similar to that of **20**, it shows a ten proton multiplet at τ 2.7, a one proton singlet at τ 3.31, a very broad two proton peak at τ 4.25 and a two proton AB quartet centered at τ 6.68, J_{AB} = 13.1 cps. The broad peak at 4.25 was assigned to the protons of the -NH$_2$ group. Later we learned that conversion of cyanides to amides has been reported by the same method[39].



20 **21**

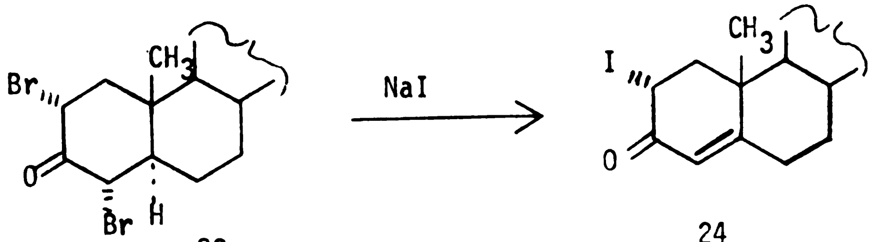
Attempted hydrolysis of the amide. An attempt was made to hydrolyze the amide 21 with dry NaOH in dimethylsulfoxide[39]. Acidification of the products gave an acid which was not the one expected (22) as judged by spectroscopic properties. All other attempts to convert the amide to the corresponding acid or methyl ester failed. These attempts included reaction of the amide with nitrous acid in fluorosulfonic acid at -78° and treatment of the product with sodium methoxide in methanol, whereby the amide was recovered along with polymeric material. Reaction of the amide with iso-amylnitrite in the presence of sodium methoxide failed.



21 22

Preparation of 1-methoxy-1,3-diphenylcyclobut-2-ene 25.

The reaction of sodium cyanide in DMSO with the dibromide made us think that there was a possibility that dehydrohalogenation of one bromine could be combined with substitution of the other. Therefore the dibromide and methanol were mixed in DMSO. This reaction was not successful since after 5 hrs, only a mixutre of dimethoxycyclobutane and starting material was obtained. Sodium iodide has been used successfully as a catalyst for displacement[40], and in a steroid system a 1,3-dibromo compound 23 was converted to 24[41].



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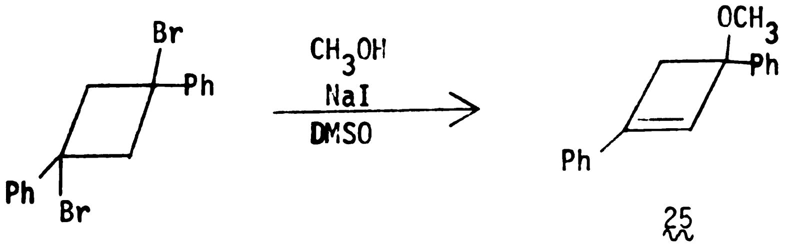
24

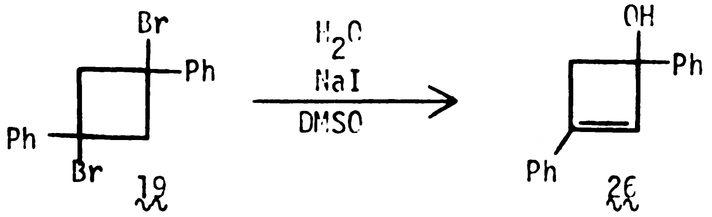
Sodium iodide and small amounts of methanol were dissolved in dimethylsulfoxide and the bromide 19 (mixture of both isomers) was added to the solution. After 8 hrs, aqueous workup and extraction with ether gave an oil obtained in almost quantitative yield. The oil showed an nmr spectrum consisting of a ten proton multiplet at τ 2.75, one proton singlet at τ 3.35, a sharp three proton singlet at τ 6.82, and a two proton AB quartet (J_{AB} = 13 cps) at τ 7.02 which was consistent with the structure 25. The ether peak in the ir spectrum is shown at 1117 cm^{-1}. The mass spectrum shows a parent peak at 236 with fragments at 221 and 191. The 191 peak was observed in the mass spectrum of almost all cyclobutene derivatives and could be due to diphenylcyclopropenium ion. The product of the reaction is pure and no further purification was needed.



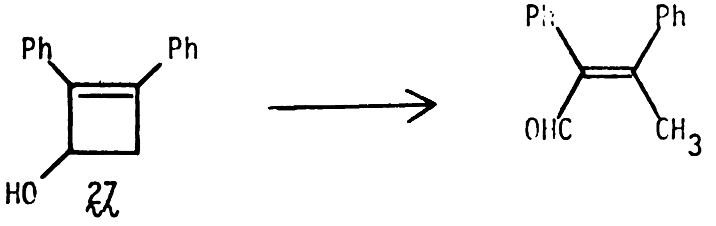
19

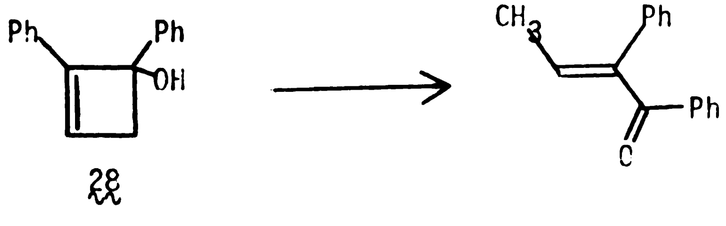
25

Preparation of 1,3-diphenylcyclobut-2-ene-1-ol 26. When it was observed that the reaction of methanol and dibromide in the presence of sodium iodide in dimethyl sulfoxide yielded the methoxy cyclobutene 25, it was reasoned that water could be used in the same manner to yield the cyclobutenol 26. Thus a mixture of the isomers 19

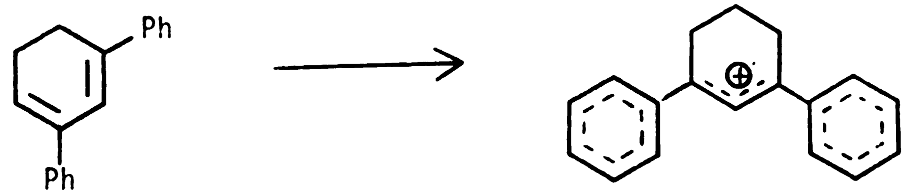


(a and b) was treated with water in dimethylsulfoxide in the presence of sodium iodide. Workup yielded the solid cyclobutenol 26 in good yield. Since the compound decomposes rapidly no analysis could be obtained. The nmr spectrum of the compound consists of a ten proton multiplet at τ 2.65, a one proton singlet at τ 3.4, a two proton singlet at τ 6.8, and a one proton peak at τ 7.45 which disappeared when the sample was shaken with D_2O. The ir spectrum shows a hydroxyl stretching vibration at 3450 cm^{-1}. Structure 23 was assigned based on the spectral evidence, and the nmr spectrum of the cation produced when the alcohol is treated with fluorosulfonic acid, which is identical with that produced from methoxycyclobutene 25. As stated, alcohols of this type (27, 28) are known to be very unstable and decompose to open chain ketones[42].





Preparation of 1,3-diphenylcyclohexenyl cation (29). This cation was prepared by direct addition of 1,3-diphenyl-1,3-cyclohexadiene 10 to fluorosulfonic acid at -78° under a nitrogen atmosphere in a concentration range of 15-20%. The nmr spectrum of the cation was determined at a temperature range of -60° to +25°. The nmr signals at lower temperature were broad due to viscosity of the solution. They started to show the expected pattern only at -20° and higher temperatures.



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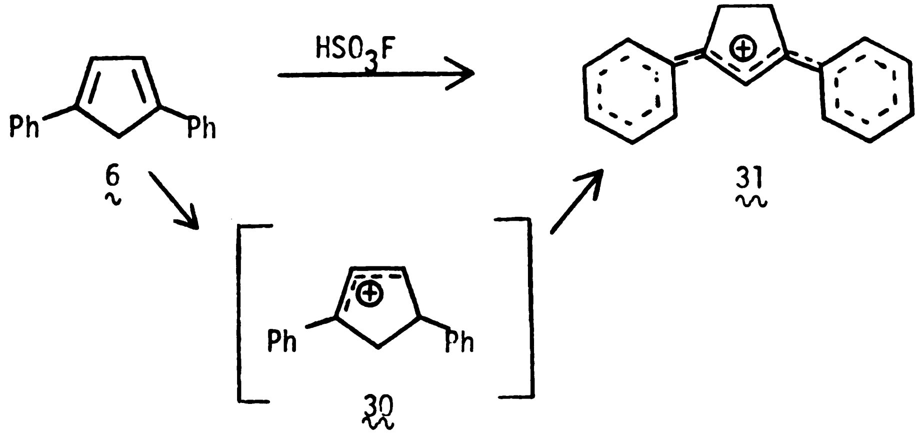
29

At room temperature the phenyl protons of cation 29 appeared at τ 1.77, 2.41 and 2.14 assigned[43] to ortho, meta and para protons respectively (Fig. 2). The rest of the spectrum is summarized in Table I.

Preparation of 1,3-diphenylcyclopentenyl cation (31). When 1,4-diphenyl-1,3-cyclopentadiene 6 was dissolved in fluorosulfonic acid cation (31) was formed. Protonation of 6 should give rise to cation (30).



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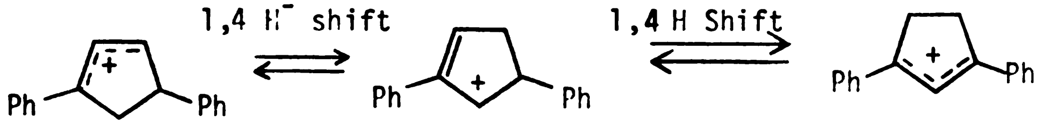
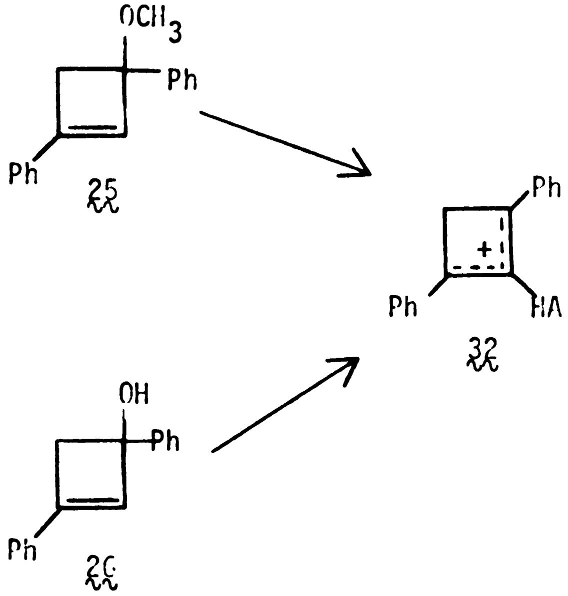
Conversion of **27** to **28** could occur by two 1,4 hydride shifts.



30 **31**

The nmr spectrum of this cation was determined over a temperature range of -60° to room temperature. The problem of broad signals at lower temperature was encountered in this case also. The cation exhibited the expected pattern for a 1,3-diphenylallylic cation at temperatures above -20° (Table I) (Fig. 3). Cations **29** and **31** had identical phenyl absorption patterns with that reported for diphenylcyclopropenium cation[43].

Preparation of 1,3-diphenylcyclobutenyl cation (**32**). This cation was prepared by addition of a Freon 114 B$_2$ solution of methoxycyclobutene **25** to fluorosulfonic acid at -78°. It was alternatively prepared by addition of a methylene chloride solution of cyclobutenol **26** to fluorosulfonic acid at -78°. The cation **32** prepared from either precursor gave



25 **32** **26**

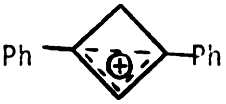
the same spectrum, except that the cation prepared from methyl ether **25** exhibited a singlet due to methanol produced in ionization of the methyl ether. The cation is stable at temperatures of -70 to +35°. At -70° the nmr showed a broad two proton doublet at τ 1.46 and a nine proton multiplet at τ 1.96, a singlet at τ 1.74 is merged with the signal at τ 1.96 (Fig. 4). On warming, the lower field signal collapsed, but the rest of the spectrum including the singlet at 1.74 sharpened up (Fig. 5). At about room temperature the lower field signal also sharpened up to a doublet of doublets at higher field than the original signal. The singlet previously observed at τ 1.74 appears as a shoulder on this doublet of doublets. At room temperature (Fig. 6) the spectrum consisted of a 5 proton doublet of doublets at τ 1.74 with area ratio of ca 1.5:3.5. The singlet one proton signal at τ 1.87, which appears as a shoulder in the second portion of the doublet of doublets, is responsible for increasing the area of the higher field doublet. Therefore the four proton signal at τ 1.75 was assigned to the ortho protons and the singlet at 1.87 was assigned to the vinyl proton H_A. The para and meta protons appear as a six proton multiplet, the signal centered at τ 1.98 was assigned to the para protons and the signal centered at τ 2.18 was assigned to the meta protons on the basis of the near identity of the spectrum with that calculated for diphenylcyclopropenium ion[43]. Collapse of the two proton doublet at τ 1.46 (at -70°) on warming and resharpening of the signal as a four proton doublet of doublets was assumed to be due to the phenyl groups not being allowed to rotate freely at low temperature, which would make the two ortho protons of each ring magnetically different. The two in the proximity of the allylic system probably appear at lower field. Warming would allow rotation to increase to a frequency comparable to that of the nmr transition. At room temperature the two *ortho* protons in each ring have the same average magnetic field because of free rotation and the position of the peak is averaged out as shown by the signal at higher field at τ 1.75.

*Comparison of cations **29**, **31**, and **32**.* Comparison of the nmr spectrum of the three cations shows a small, but perhaps significant downfield shift of the phenyl protons in going from system **26** to **29** while the methine proton of the allylic system shows a gradual upfield shift (with the exception of the special case of the cyclopropenyl cation) (Table I).

Table I: Chemical Shifts for 1,3-diphenylcycloalkenium ions (τ)

Cation/H	*ortho*	*para*	*meta*	methine	Other protons
cyclohexenyl	1.77	2.14	2.41	1.46	6.42 (t,J=6.5 cps,4H) 7.64 (q,J=6.5 cps,2H)
cyclopentenyl	1.76	2.10	2.35	1.51	6.04 (s, 4H)
cyclobutenyl	1.75	1.98	2.18	1.87	5.82 (s, 2H)
cyclopropenyl[43]	1.55	1.92	2.10	-0.45	

If the bicyclobutyl cation **30** were a major resonance contributor the reverse trend would have been expected. Namely the closer C_1 and C_3 get the more 1,3-overlap would be expected. This would lead to less participation of the phenyl in the stabilization of the cation and concentration of more positive charge on C_2. As observed this was not the case. An alternative is dismissal of the presence of such contribution



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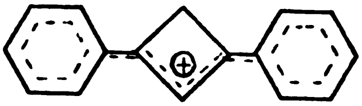

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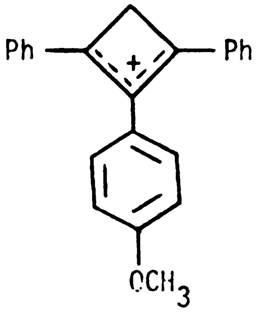
and distribution of the charge as expected for the 1,3-diphenylallylic system **31**. This, however, doesn't explain the low field shift trend from **26** to **29** and upfield shift of the methine proton from τ 1.46 to τ 1.87. Although the shifts are small, nevertheless, they exist. The fact that the trend is correlated with a decrease in ring size suggests the possibility that there is an electrostatic repulsion between the positive charges which tends to disperse them as far away from each other as possible. This, however, doesn't exclude the possibility of the presence presence of 1,3-π overlap. It only implies that if there is such overlap it is not the predominant factor in determining the chemical shifts. The upfield shift of the methine protons could be the result of the altered geometry in the smaller ring accompanied by less deshielding of the methine proton by the phenyls.

The 1,3-diphenyl is not the best system to study the possibility of 1,3-π overlap. Thus the predicted delocalization energy gained by this process (4.1 - 10 kcal/mole[1]) is perhaps not sufficient to balance any

loss of the delocalization energy contributed by the phenyl rings. A better system perhaps would be 1,3-diphenyl-2-*p*-methoxyphenylcyclobutenyl cation **32** where the *p*-methoxyphenyl could stabilize the positive charge placed on C_2 by 1,3-π overlap.



The fluorine nuclear magnetic resonance deshielding of *p*-fluorophenyl carbonium ions has been shown to be related linearly to the stabilization energy of *para*-substituted triphenylmethyl cations[44]. A series of unpublished results from this laboratory have confirmed *p*-fluorine is a more sensitive probe for determination of charge distribution in the phenyl ring as compared with the *p*-proton[45]. Thus, in order to avoid a probable uncertainty caused by the small change in chemical shift of the *p*-protons, we suggest that the *p*-fluorophenyl analogues of these cations be used in further studies.

EXPERIMENTAL

Preparation of 3-phenylcyclopent-2-enone, 1. (a) Condensation. Ethyl acetoacetate (26 g, 0.2 mole) in dry benzene (250 ml) was added to sodium hydride (9.6 g of 50% dispersion in oil) in benzene and the mixture was stirred under a nitrogen atmosphere. After the completion of the reaction (indicated by cessation of bubbling of hydrogen), phenacyl bromide (40 g, .20 mole) was added at once and the mixture was refluxed for six hrs. The reaction mixture was then washed with cold water twice (total of 800 ml). The benzene solution was dried over magnesium sulfate and evaporated to give an oil the nmr spectrum of which exhibited peaks characteristic of ethylbenzoylpropionate and 1-phenyl-3-carbethoxypentane-1,4-dione **2**.

b) Saponification and decarboxylation. The product of the above reaction was placed in a three liter flask, an 0.8% solution of potassium hydroxide (2.5 l) was added, and the mixture was refluxed under a nitrogen atmosphere for 2.5 hrs. The reaction mixture was then cooled and extracted with ether. The ether solution was washed with water and dried over magnesium sulfate. Evaporation of the ether gave a brownish oil which was chromatographed on an alumina column. The diketone 3 (1-phenylpentane-1,4-dione)(7g) was eluted first with ethyl acetate-benzene (20:80). A mixture of the diketone and the cyclopentenone (7.5 g) followed by the cyclopentenone (4.5 g) was eluted with ethyl acetate. The diketone was separated from the mixture by distillation: (bp 104° at 0.35 mm); ir 1720 cm^{-1}, 1695 cm^{-1}: nmr

(CCl_4) 2.2 (m, 2H), 2.68 (m, 3H), 7.16 (A_2B_2, q, 4H), 7.97 (s, 3H). 3-Phenylcyclopentenone (2 g) was obtained from the residue by crystallization from hexane-ether.

c) *Ring closure*. The combined diketone crop (12 g) was refluxed in aqueous potassium hydroxide (250 ml of a 10% solution) under a nitrogen atmosphere for 2 hrs to give 9.5 g of a light brownish phenylcyclopentenone isolated by chromatography as above, giving a total overall yield of 52%. The pure ketone **1** was obtained by sublimation of the crude product: mp 83.5 - 84.5°; ir (CCl_4) 1705-1695 cm^{-1}; nmr ($CDCl_3$) 2.6 (m, 5H), 3.6 (t, J = 1.5 cps, 1H), 7.05 (m, 2H), 7.55 (m, 2H).

Preparation of 1,4-diphenyl-1,3-cyclopentadiene (6). Ketone **1** (3.16 g, 0.02 mole) in ether (20 ml) was added to phenyl Grignard prepared from bromobenzene (3.3 g, 0.021 mole) and magnesium turnings (50 mg) in ether under an argon atmosphere. After 3 hrs the reaction was worked up by adding concentrated ammonium chloride solution. The ether solution was washed with water and evaporated to give an oil, which was dissolved in warm methanol. When the methanolic solution was chilled, 2.9 g (35%) of solid was obtained: mp 155.5 - 157° (lit[8] 155-157°); nmr ($CDCl_3$) τ 2.6 (m, 10H), 3.12 (t, J = 1 cps, 2H), 6.27 (t, J = 1 cps, 2H).

Preparation of 3-phenylcyclohex-2-enone (7). (a) *Michael Condensation*. This reaction was done according to Walker[10]. A 40% methanol solution of Triton B (60 ml) was added to a stirred solution of ethyl benzoylacetate (56.75 g, 0.295 mole) and methylvinylketone (20.75 g, 0.296 mole) in t-butyl alcohol (75 ml) at 0°. The solution became brownish and then green. After 5 hrs the reaction was worked up according to Walker to give a mixture of crystalline material and oil. The mixture was triturated with ether and filtered to give 39.5 g of a crystalline compound **8**, mp 122-125°, which, when recrystallized from methanol, had mp 125-127° (lit.[10] 128-130°); ir (Nujol) 3400 cm^{-1}, 1707 cm^{-1}, 1693 cm^{-1}; nmr ($CDCl_3$) τ 2.7 (m, 10), 5.79 (b.s., 1H), 6.05 (q, 2H), 7.4 (s, 2H), 7.55 (m, 4H) and 9.02 (t, 3H). The filtrate when evaporated yielded 29.7 g of a yellow brown oil, **9**.

b) *Decarboxylation of the condensation products*. The solid obtained from above (31.5 g) was treated with an 8% aqueous potassium hydroxide solution (250 ml) and refluxed for 12 hrs. The mixture was then cooled and extracted with ether, which was washed with water and dried over magnesium sulfate. Evaporation of the solvent resulted in 19.1 g of the product which was recrystallized from hexane-ether (80:20) to give 17.5 g of the ketone: mp 64.5-65.5° (lit. 64-65°); ir 1665 cm^{-1}: nmr ($CDCl_3$) τ 2.7 (m, 5H), 3.64 (t, J = 1.5 cps, 1H), 7.13-8.1 (complex m, 6H). The brown oil (29.1 g) obtained in (a) was refluxed in 8% potassium hydroxide (250 ml) to give the desired ketone (7.5 g) as a brownish solid. This crude product when recrystallized from hexane-ether (80:20) gave 6.1 g of the pure ketone **7**. The total yield of pure ketone was 23.6 g (46.5%).

Preparation of 1,3-diphenyl-1,3-cyclohexadiene (10). 3-Phenyl-2-cyclohexenone (6 g) in dry tetrahydrofuran was added to a Grignard Reagent prepared from bromobenzene (18.3 g) and magnesium turnings (2.8 g) in dry ether (150 ml) under an argon atmosphere. The reaction was allowed to go on overnight and then worked up by addition of a concentrated solution of ammonium chloride. The organic layer, after drying over magnesium sulfate, was evaporated to give 5.7 g of a thick yellow oil which was taken up in

95% ethanol and the solution chilled to give white platelets mp 89-93°. Recrystallization from 95% ethanol resulted in 4.9 g (66%) of the same type of crystals: mp 95-97° (lit.[11] 98-99°); nmr ($CDCl_3$), 2.67 (m, 10H), 3.33 (sextet, J = 1.5 cps, 1H), 3.9 (dt, J = 1.5 cps, J = 4.5 cps, 1H), 7.4 (m, 4H).

Photodimerization of trans-cinnamic acid. Practical cinnamic acid (145 g) was placed in a 5 liter two neck round bottom flask which was used as the photolysis apparatus. The two joints are ₮ 55/60 and 24/40 size. Water (500 ml) was added to the cinnamic acid, and the suspension was stirred mechanically to obtain a more thorough suspension. A Pyrex photolysis insert was introduced into the wider joint. Water (4 liter more) was added through the side joint and a mechanical stirrer fitted with a Teflon paddle (1 inch long) was inserted in such a way as to avoid contact with the jacket or the walls of the flask during stirring. A football shape magnetic bar was used to stir the suspension from the bottom. The suspension was irradiated with a 550 watt Hanovia lamp. The cinnamic acid gathered on the top at first, but a very good suspension was formed gradually as the reaction proceeded. After 5 days the reaction was stopped. The suspension was filterd and air dried on the Buchner funnel. The dried solid was washed several times with ether (total 1200 ml) to remove the unreacted cinnamic acid and dried in an oven at 60° for one hr. The solid was placed in a one liter beaker, triturated with boiling ether, and filtered to give 81.5 g of α-truxilic acid **14** (56.2%) mp 280-285° (lit.[1] 280-281.5°). The crude material gives 72 g of pure acid, mp 290-291°.

Preparation of truxilloyl chloride. This compound was prepared according to E. H. White[21]. Treatment of truxillic acid (29.6 g, 0.1 mole) with thionyl chloride (300 ml) yielded crystalline acid chloride. Recrystallization from benzene-pet ether (60:40) gave white prisms (26.7 g,81%): mp 121-123°; ir (Nujol) 1785 cm^{-1}.

Preparation of di-t-butylpertruxillate (18). Truxilloyl chloride (22 g) was mixed with t-butylhydroperoxide (40 ml) in dry benzene, under a nitrogen atmosphere. The mixture was cooled in an ice-salt bath to 0° and dry pyridine[47] (25.0 ml) was added dropwise. The reaction mixture was allowed to stir for 12 hrs. The contents of the flask were then washed with 5% hydrochloric acid in ice water to remove the excess of pyridine. The unreacted acid and traces of hydrochloric acid were removed by washing with potassium hydroxide solution (150 ml of a 5% solution). The organic layer was dried over magnesium sulfate and solvent evaporated under reduced pressure at room temperature. The solid residue (25.5 g) was recrystallized from ether-hexane (1:2) (150 ml). The resulting needles weighed 23.7 g (81.5%): mp 142-142.5°; ir (Nujol) 1750 cm^{-1}.

Titration of di-t-butylpertruxillate. Two samples of perester (200 mg each) were dissolved in chloroform (15 ml for each). Ferric chloride solution in acetic acid (20 ml of a 0.002% solution) and sodium iodide (2 g) was added to each[48]. Both samples were kept in the dark for 10 minutes and then immediately titrated with 0.1N solution of sodium thiosulfate to the end point as indicated by starch indicator. A blank solution containing the same ingredients except for the perester was run.

The two samples consumed 18.5 and 18.4 ml of standard thiosulfate and 1.1 ml of thiosulfate was necessary for the blank.

$$\text{mole perester} \longrightarrow 2I_2 \longrightarrow 4 \text{ mole } Na_2SO_3$$

$$\frac{17.4}{4} \times 10^{-4} = 4.35 \times 10^{-4} \quad \text{mole of perester}$$

$$4.35 \times 440 \times 10^{-4} = 0.1914 \text{ g of pure perester in 0.2 g of crude perester}$$

$$\frac{0.1814}{0.20} \times 100 = 95.7\% \text{ active perester}$$

Pyrolysis of di-t-butyl pertruxilate. The perester (22.5 g) was suspended in *p*-cymene (600 ml of solvent, distilled at 207.5-208.5°) and the suspension was heated under a stream of nitrogen with stirring. The perester dissolved at around 55°. At 130° the solution turned yellowish and effervescence began which became vigorous at around 150°. After 1.5 hrs the bubbling stopped, but heating was continued for 12 more hrs. The yellowish solution was then attached to a 36" vigreaux column and the bulk of the *p*-cymene was distilled (at 35°, 0.5 mm). The yellow pasty residue was taken in ethanol and chilled. The *p*-cymene dimer which crystallized was filtered off and the mother liquor was stripped of sovlent and distilled through a 4 inch Vigreaux column. *p*-Cymene was distilled first. The fraction which distilled at 125-140°, 1.00 mm was rich in the desired product (70-80% as judged by nmr). The residue of distillation also contained 20-30% of the product. The above mentioned fraction and the residue were combined and redistilled to give 5.8 g of an oil (110-123° at 0.25 mm) containing 90% of the cyclobutane **13**.

Column chromatography over silicic acid yielded 4.5 g (42%) of pure hydrocarbon as a thick oil. Recrystallization from methanol yielded needles: mp 40-41°; ir (film) 3030, 2980, 1610, 1500, 1450 cm^{-1}; nmr (CCl_4) τ 2.8 (m, 10H), 6.4 (q, J = 7 cps, 2H), 7.48 (t, J = 7 cps, 4H).

Anal. Calcd. for $C_{16}H_{16}$: C, 92.26; H, 7.74;

Found: C, 92.07; H, 7.60.

Preparation of 1,3-dibromo-1,3-diphenylcyclobutane, (19).

1,3-Diphenylcyclobutane (2.2 g, 105 mmole) was dissolved in carbon tetrachloride (50 ml) and N-bromosuccinimide (4.3 g, 2.31 mmole) and benzoylperoxide (0.2 g) were added. The mixture was brought to reflux by means of an oil bath. When all of the n-bromosuccinimide was consumed the succinnimide was filtered and the solvent was removed at reduced pressure. The residue was taken up in ether. The ethereal solution yielded needles (800 mg): mp 145-145.5° (dec); nmr ($CDCl_3$) τ 2.6 (m, 10H), 5.85 (s, 4H).

Anal. Calcd. for $C_{16}H_{14}Br_2$: C, 52.46; H, 3.83; Br, 43.71;

Found: C, 52.62; H, 3.94; Br, 43.65.

Addition of hexane to ethereal mother and cooling gave a solid (1.9 g) (total yield 69%) which was a mixture of the solid previously obtained and another substance which showed nmr ($CDCl_3$) τ 2.7 (10H), 6 (s, 4H).

Anal. Calcd. for $C_{16}H_{14}Br_2$: C, 52.46; H, 3.83; Br, 43.71;

Found: C, 52.62; H, 3.82; Br, 43.62.

Both isomers decompose when allowed to stay in air.

Preparation of β-nitrostyrene. The title compound was prepared according to the organic synthesis preparation[46]. In this preparation benzaldehyde (530 g, 5 moles), nitromethane (305 g, 5 moles) and sodium hydroxide (500 ml of a 50% aqueous solution) were used. The yield of crude material was 580 g (77.8%). Recrystallization from hexane yielded long needles: mp 56.5-57.5° (lit.[47] 57-58°).

Photodimerization of β-nitrostyrene. β-Nitrostyrene (76.5 g) was placed in an 18 inch open crystallization dish and water (800 ml) was added. A water bath cooled to 18°C by passage of tap water through copper coils installed in it was used to cool the suspension. A mechanical stirrer fitted with a 3 inch Teflon paddle was used to stir the suspension. A 550 watt Hanovia lamp in a Pyrex water cooled jacket placed horizontally on the top of the crystallization dish was used to irradiate the suspension. After 24 hrs the irradiation was stopped and the suspension was filtered and washed by soxhlet extraction with hexane to yield 59 g (77%) of crude 1,3-dinitro-2,4-diphenylcyclobutane: mp 175-181°. Recrystallization from benzene gave 41.3 g (54%) of pure dimer **14**: mp 183-185° (lit.[28] 181-182°); ir (Nujol) nmr ($CDCl_3$) τ 2.68 (m, 10H), 6.6 (A_2B_2 system, 4H).

Reductive alkylation of 1,3-diphenyl-2,4-dinitrocyclobutane (15). The dinitro compound **14** (45 g, 1.51 mole) was placed in a three liter round bottom flask and zinc dust (300 g) and formaldehyde (250 ml of a 37% aqueous solution) were added. The suspension was warmed on a steam bath and formic acid (550 ml of a 88% aqueous solution) was added dropwise over a period of 4 hrs with vigorous stirring. As soon as the reaction started the external heat was discontinued since heat of reaction was sufficient to maintain the temperature at about 80-90°. After the addition was completed the reaction was heated over a steam bath again for 6 hrs more, and formic acid (200 ml in 2 portions) was added to ensure completion of the reaction. The insoluble material was then filtered and the filtrate was concentrated under reduced pressure at 60°. The concentrated solution was extracted with benzene and the aqueous phase was made basic with sodium hydroxide solution. A white precipitate formed which was filtered and the solid was washed with ether. The filtrate was also extracted with ether. The combined ethereal solution was washed with water, and dried over magnesium sulfate. Evaporation of ether yielded 38.5 g of a white solid, which was recrystallized from ether-hexane (20:80) to give 35.5 g (79.9%) of pure **15**: mp 125-127° with spectroscopic properties identical to those reported below.

Preparation of 1,3-diphenyl-2,4-bis(dimethylamino)cyclobutane.

Truxilloyl chloride (26.7 g, 0.08 mole) was treated with activated sodium azide (38.0 g, 0.58 mole), in dry benzene (200 ml) according to White[31] To the di-isocyanate (ir Nujol 2280) obtained in this manner formic acid (400 ml of 85% solution) and formaldehyde (120 ml of 35% aqueous solution) were added. The mixture was heated at 60° for 24 hrs. The solution was then cooled and made basic with sodium carbonate solution and was extracted with ether. After removal of ether a solid material was obtained which was sublimed. Recrystallization of the sublimed material from ether hexane (20:80) gave large crystals: (10.6 g, 45.8%) mp 124-125° (lit.[31] 122-123°); ir ($CHCl_3$) 2990, 2950, 2850 and 2800 cm^{-1}; nmr ($CDCl_3$) τ 2.75

(m, 10H), 6.7 (A_2B_2 q, 4H), 8.25 (s, 12H). Truxillic acid (2 g) was recovered from acidification of the basic aqueous solution.

Preparation of 1,3-diphenyl-2,4-*bis*-(dimethylamino)cyclobutane-dimethiodide (16) 2,4-Diphenyl-1,3-*bis*(dimethylamino)cyclobutane (6.7 g) was dissolved in anhydrous acetone (50 ml) with a little warming. Methyl iodide (10 ml) was added and the mixture was warmed for 2 minutes. The flask was stoppered and allowed to stand for half an hour. The dimethiodide was filtered and proved to be pure without any need for recrystallization: mp 222-225° (lit.[31] 215-217°).

Reductive deamination of bis-methiodide 16. *bis*-Methiodide **16** (14 g, 0.024 mole) was added to distilled liquid ammonia (400 ml) at -78°, isopropanol (3.6 ml) was added and lithium ribbon (washed with pet ether to remove the oil) was cut and added in pieces until the blue color persisted for 2 minutes. The mixture was then allowed to stir at -78° for 30 more minutes.and then ammonium chloride (10 g) was added. Ammonia was then allowed to evaporate and the residue was taken in ether, and washed with water and then hydrochloric acid solution. The ether solution was dried and evaporated to give a yellow fluorescent oil. The oil was distilled (91° at 0.15 mm) to give 3 g of a clear liquid, the nmr spectrum of which showed peaks characteristic of 1,3-diphenylcyclobutane plus some other material. The mixture could not be separated by gas liquid chromatography, column chromatography or fractional distillation, and was successfully used in the preparation of dibromide **19**.

Reaction of 1,3-dibromocyclobutane (19) with methanol in the presence of sodium iodide. The dibromo cyclobutane (A) (150 mg) was dissolved in methanol (100 ml) and sodium iodide (1 g) was added. The solution was stirred under a nitrogen atmosphere. After 8 hrs the mixture was poured into cold water (500 ml) and the aqueous solution was extracted with ether. The ethereal solution was washed with water and dried over magnesium sulfate. Evaporation of the ether afforded a yellow oil (110 mg). The product showed spectral properties similar to those of the product of the reaction of dibromocyclobutane with sodium methoxide (see below).

Treatment of the dibromocyclobutane with sodium bicarbonate. The dibromocyclobutane (A) (200 mg) was dissolved in dry tetrahydrofuran (50 ml) and sodium bicarbonate (300 mg) was added. The mixture was stirred under a nitrogen atmosphere and maintained at 40-50° by means of a water bath. Filtration of the mixture and evaporation of the solvent yielded starting material (180 mg) which had spectral properties identical with those of an authentic sample.

Attempted preparation of 1,3-diphenylcyclobut-2-enyl cation. The dibromocyclobutane (**11**) (100 mg) in methylene chloride (5 ml) was added to a mixture of antimony pentafluoride (0.2 ml) and fluorosulfuric acid (1.1 ml) at -78° under an argon atmosphere. The nmr spectrum of this solution over a range of temperature (-70° to -10°) shows a multiplet 1.7-2.6 ppm upfield from fluorosulfuric acid signal, and a singlet at 7 ppm upfield from the same signal in an area ratio of 15:2.

Reaction of dibromocyclobutane with sodium methoxide. The isomer (A) (150 mg) was dissolved in dry methanol (25 ml) and powdered sodium methoxide (350 mg) was added. The mixture was stirred under nitrogen for 5 hrs at room temperature. The reaction mixture was then added to water (200 ml) and extracted with ether (250 ml). The ethereal solution was washed with water and dried over magnesium sulfate. Evaporation of the ether gave a yellowish oil whose nmr spectrum included signals characteristic of 1,3-dimethoxy-1,3-diphenylcyclobutane.

Preparation of 1,3-diphenylcyclobut-2-enyl cyanide(21)

1,3-Dibromo-1,3-diphenylcyclobutane (2 g, 5 mmole) (A) was dissolved in acetonitrile (150 ml) and dimethylsulfoxide (60 ml) under a nitrogen atmosphere. Sodium cyanide (2 g) was added to the solution and the mixture was stirred at room temperature for 10 hrs. The milky yellow solution was then poured into one liter of water and extracted with ether (twice 300 ml). The ethereal solution was washed with water several times and then with saturated sodium chloride solution and was dried over magnesium sulfate. Evaporation of the solvent yielded a brownish oil which was chromatographed on Fluorisil. The desired product was eluted with hexane as a yellow oil (1.03 g, 81.66): ir (neat) 2220 cm^{-1}; nmr (CCl_4) 2.70 (m, 10H), 3.72 (s, 1H), 6.79 (A_2B_2 q, J = 13 cps, 2H). In another run 4 g of a mixture of isomers A and B of the dibromocyclobutane gave 2.15 g, of the product.

*Preparation of 1,3-diphenylcyclobut-2-ene-1-carboxamide (**22**).* Sodium methoxide (commercial powder 1.2 g) was dissolved in dimethylsulfoxide (50 ml). Compound **21** (1.1 g, 4.7 mmole) in dimethylsulfoxide (5 ml) was added. The solution was stirred at room temperature under a nitrogen atmosphere. After 48 hrs, the solution was poured into 800 ml ice water and extracted with ether. The ether solution was washed with water several times and dried over magnesium sulfate. When the ether solution was concentrated to 15 ml and hexane was added a white precipitate formed which was filtered and recrystallized from hexane-ether to give 0.872 g (73%) of a white solid: mp 143-145°; ir ($CHCl_3$) 3500, 3360, 1685 cm^{-1}; nmr ($CDCl_3$) τ 2.7 (m, 10H), 3.31 (s, 1H), 4.25 (broad, 2H), 6.68 (A_2B_2 q, J = 13.1 cps, 2H).

*Preparation of 3-methoxy-1,3-diphenylcyclobutene (**23**).* Sodium iodide (3 g) was dissolved in dimethylsulfoxide (50 ml) and absolute methanol (1.5 ml) was added to the solution. 1,3-dibromo-1,3-diphenylcyclobutane (1.5 g of the mixture of isomers) was dissolved in 5 ml of dimethylsulfoxide and added to the solution. After a while a yellow color developed which gradually turned red-brown (iodine). After 12 hrs the solution was added to ice water (800 ml), and the cloudy solution was extracted with ether. The ether solution was washed with a dilute sodium sulfite solution to remove the iodine and washed several times with water to remove the dimethylsulfoxide. The ether solution was dried and evaporated to give 0.953 g (98.5%) of an oil: ir ($CHCl_3$) 1117 cm^{-1}; nmr (CCl_4) τ 2.75 (m, 10H), 3.35 (s, 1H), 6.82 (s, 3H), 7.02 (A_2B_2 q, J = 13 cps, 2H); m/e 236.

Preparation of 1,3-diphenylcyclobut-2-ene-1-ol (**26**).

Cyclobutanedibromide (**19**) (0.500 g) was dissolved in a solution of sodium iodide (1 g) and water (1 ml) in dimethylsulfoxide (50 ml) at room temperature. After 8 hrs the solution was poured into water (800 ml) and extracted with ether. The ether solution was washed with water and dried over magnesium sulfate. Evaporation of the ether yielded a solid with a broad mp range: ir ($CHCl_3$) 3600 cm^{-1}; nmr ($CDCl_3$) τ 2.65 (m, 10H), 3.4 (s, 1H), 6.8 (s, 2H), 7.45 (bs, 1H); mass spectrum: intense peak at 205 corresponding to 1,3-diphenylcyclobutenium ion.

Preparation of trans-2-phenylcyclopropylcarboxylic acid.

(a) Preparation of γ-phenyl-γ-butyrolactone (**34**). This compound was prepared according to Julia[48] from β-benzoylpropionic acid (252 g). After workup a colorless oil (207.4 g, 83%) was obtained: bp 142-3°, 2.5 mm; ir (neat) 1780 cm^{-1}; nmr (CCl_4) τ 2.8 (s, 5H), 4.7 (dd, J = 8 cps, J = 7 cps, 1H), and 7.5-8.5 (complex m, 4H).

(b) Preparation of ethyl-γ-chloro-γ-phenyl butyrate (**35**). The lactone from part (a) (32 g) was treated with thionyl chloride (73 g) in dry benzene and the γ-chloro acid chloride obtained was treated with acidic ethanol according to Julia. The yield of distilled product was 38 g (62%): ir (neat 1720 cm^{-1}; nmr (CCl_4) τ 2.7 (m, 5H), 5.05 (m, 1H), 6.0 (q, 2H), 7.8 (m, 4H), 8.8 (t, 3H).

(c) Preparation of ethyl-trans-2-phenylcyclopropylcarboxylate (**36**). The chloro ester obtained in (b) (26 g, 0.11 mole) was cyclized by treatment with a sodium t-amylate solution. Workup resulted in 12.3 g (56%) of the product as a colorless liquid which solidified in the refrigerator to give crystals: mp 31-33°; ir (neat) 1719 cm^{-1}; nmr (CCl_4) τ 2.9 (m, 5H), 5.92 (q, 2H), 7.56 (octet, J_1 = 7.5 cps, J_2 = 6 cps, J_3 = 4.5 cps, 1H), 8.03-8.8 (m, 3H), 8.78 (t, 3H). This ester was converted quantitatively to the corresponding acid by refluxing in methanolic potassium hydroxide for 5 hrs. The crude acid mp 84-86° on recrystallization from hexane gave colorless light crystals: mp 90-91°; ir (Nujol) 1700 cm^{-1}; nmr ($CDCl_3$) τ 2.8 (m, 5H), 7.4 (octet J_1 = 10 cps, J_2 = 7 cps, J_3 = 4 cps, 1H), 7.95-8.85 (m, 3H).

Preparation of trans-1-benzoyl-2-phenylcyclopropane

(a) trans-2-Phenylcyclopropylcarboxylchloride (38). The acid (20 g) was treated with thionyl chloride (40 ml) in refluxing dry benzene (100 ml) for 4 hrs. The thionyl chloride and benzene were then removed under reduced pressure and the residue distilled (104° at 1.5 mm) to give 18.05 g (88%) of the acid chloride as a yellow liquid (1).

(b) Diphenylcadmium reaction. Dried cadmium chloride (39 g, 0.21 mole) was added to a Grignard Reagent prepared from bromobenzene (64.8 g, 0.42 mole) and magnesium turnings (9.8 g, 0.48 m) in dry ether (180 ml). The mixture was refluxed for one hour with stirring. The ether was then distilled off, dry benzene (220 ml) was added to the solid residue, and the mixture was heated to the boiling point of benzene. This mixture was cooled to 10° and trans-2-phenylcyclopropylcarboxyl chloride (18.05 g, 0.109 mole) in dry benzene (15 ml) was added dropwise with vigorous stirring. The reaction mixture was then refluxed for 3 hrs.

The thick suspension was then poured on ice-dilute (10%) hydrochloric acid solution and extracted with ether. The ether solution was washed with dilute sodium hydroxide solution (to remove the acid) and washed with water and dried over magnesium sulfate. Evaporation of the ether yielded 15.2 g (66%) of the ketone 39 in the form of a liquid. An attempt to distill the product caused decomposition of the ketone. The liquid shows the following spectroscopic properties: ir (neat) 1665 cm^{-1}; nmr (CCl_4) τ 2.15 (m, 2H), 2.7 (m, 8H), 7.3 (m, 2H), 8.2 (octet, J = 3 cps, J_2 = 6 cps, J_3 = 11 cps, 1H), 8.7 (sextet, $\Delta\nu$ = 3 cps, 1H). Crystallization of the ketone from hexane ether (80:20) yielded crystals mp 30-36° which had the same spectroscopic properties.

Preparation of 1-benzoyl-2-phenylcyclopropane (39). The title compound was prepared according to Corey[49]. Benzalacetophenone (31.2 g, 0.15 mole) in dry dimethylsulfoxide (75 ml) was added to dimethylsulfoxonium methylide prepared from trimethylsulfoxonium iodide (35.25 g, 0.16 mole) and sodium hydride (6.1 g of a 55% dispersion in oil) in dimethylsulfoxide (175 ml). Workup according to Corey[47] yielded a yellowish oil which still contained the oil from sodium hydride. The product was taken up in acetonitrile and washed with hexane to remove the oil. Evaporation of the acetonitrile yielded an oil which solidified in the refrigerator. Recrystallization from hexane afforded a solid (29 g, 87%): mp 40-58°; ir (Nujol) 1670 cm^{-1} nmr (CCl_4) τ 2.15 (m, 2H), 2.7 (m, 8H), 7.3 (m, 2H), 8.2 (m, 1H), 8.7 (m, 1H) 3 g of a yellow oil was obtained from the mother liquor with the same spectroscopic properties.

Preparation of 1-benzoyl-2-phenylcyclopropane tosylhydrazone (40). Crude 1-benzoyl-2-phenylcyclopropane (15 g, mp 39-48°) was added to p-toluenesulfonylhydrazide (27.9 g, 0.15 mole) in 95% ethanol (250 ml), and p-toluenesulfonic acid (1 g) was added to the mixture. The mixture was refluxed for 24 hrs. Concentration of the produced solution and chilling yielded 24 g of white solid mp 139-146°. When this solid was recrystallized from 95% ethanol, it gave light needles, mp 152-155° (18.5 g, 68%).

Anal. Calcd. for $C_{23}H_{22}N_2O_2S$: C, 70.76; H, 5.64; N, 7.18; S, 8.20;

Found: C, 70.79; H, 5.74; N, 7.48; S, 8.56.

Preparation of *cis*- and *trans*-α-Phenylcinnamic acid. The mixture of *cis* and *trans* acid was prepared according to the organic synthesis[51] preparation. A recipe of phenylacetic acid (109.2 g) benzaldehyde (81 ml) and triethylamine (80 ml) in acetic anhydride (160 ml) yielded the mixture of acids. The product was dissolved in an appropriate amount of sodium hydroxide and the basic solution acidified with acetic acid. The resulting precipitate was filtered, washed with water, and recrystallized from 95% ethanol to give the cis-α-phenylcinnamic acid **41** mp 169-173° (103 g) (lit.[51] 172-173°). Hydrochloric acid was added to the filtrate to lower the pH of the solution to 3 (as indicated by congo red paper). A precipitate formed which was filtered, washed with water, and recrystallized from hexane-ether (50-50) to give the *trans* acid **42** (20 g) mp 135-137° (lit.[51] 136-137°) (total yield 68%).

Preparation of α-phenylcinnamonitrile (43). The title compound was prepared according to Organic Synthesis[52]. Benzaldehyde (106 g) and benzyl cyanide (117 g) were used as starting materials. The yield was 150 g of solid (73%) mp 86-87° (lit.[52] 88°).

Preparation of 1,2-diphenylcyclopropyl cyanide (44). Trimethyl sulfoxonium iodide (66 g, 0.3 mole) was dissolved under a nitrogen atmosphere in dry dimethylsulfoxide (400 ml) with a little warming. Sodium hydride (15.5 g of a 50% dispersion in oil, 0.3 mole) was added gradually with stirring. When the evolution of hydrogen ceased, α-phenylcinnamonitrile (48.2 g, 0.24 mole) in dry dimethylsulfoxide (150 ml) was added dropwise. After the addition of nitrile was over the temperature of the reaction was raised to 50-55° by means of a water bath[53]. The reaction was continued for 2 more hrs. The reaction mixture was then poured on ice (200 g), to give a precipitate which was filtered and triturated with hot methanol. The methanolic solution was diluted with water and extracted with chloroform. When the solution was dried and the solvent evaporated, an oily solid was obtained which was recrystallized from hexane-ether (50-50) to give 34.2 g (65%) of solid mp 57-59°. Recrystallization from methanol raised the mp to 60-61° (lit. 58-60°[51]). The material which was not dissolved by trituration weighed 11.3 g and had mp > 300°. The purified product had: ir (nujol) 2230 cm^{-1}; nmr (CCl_4) τ 2.72 (broad, s, 10H), 7.48 (dd, $J_1 = 7$ cps, $J_2 = 9$ cps, 1H) 8.09 (m, 2H).

Hydrolysis of 1,2-diphenylcyclopropyl cyanide. The nitrile (5.26 g, 0.024 mole) in diethylene glycol (5 ml) and potassium hydroxide solution (1.4 g in 10 ml glycol) were mixed and refluxed under nitrogen for 72 hrs[54]. The dark brown solution was then diluted with water and extracted with ether to remove the unreacted nitrile. Acidification and extraction with chloroform gave brownish crystals (1.4 g) (24.7%) of acid **45** mp 218-222°. Recrystallization from 95% ethanol gave colorless crystals mp 224-227° (lit. 220-222°[2]). In another run 17 g of the cyanide yield 5.8 g of the same acid.

Preparation of methyl *cis*-α-phenylcinnamate (46). A solution of diazo methane in ether (300 ml) prepared from EXR101 (Dupont)[55] was added to *cis*-α-phenylcinnamic acid (30 g) in tetrahydrofuran (150 ml). After one-half hour the solution was washed with sodium carbonate solution and then with water and dried over magnesium sulfate. Evaporation of the solvent and recrystallization of the residual solid from hexane yielded 29.2 g (91.5%) of needles: mp 76-77°; ir (CCl_4) 1705 cm^{-1}; nmr (CCl_4) τ 2.33 (s, 1H), 2.86 (m, 5H), 3.05 (s, 5H), 4.37 (s, 3H).

Preparation of 1,2-diphenylcyclopropylcarboxylic acids (A) and (B). Sodium hydride (6.54 g of a 56% dispersion in oil) was added to trimethylsulfoxonium iodide (33 g, 0.15 mole) in dry dimethylsulfoxide (150 ml) with vigorous stirring under nitrogen until hydrogen evolution stopped. A solution of methyl *cis*-α-phenylcinnamate (28.56 g, 0.12 mole) in dimethylsulfoxide (100 ml) was added dropwise to the methylide over a period of one hour. The viscous solution was stirred for one hour more and poured on ice water. Extraction with ether and drying and evaporation of the ether yielded a yellow oil. The product still contained the oil from the sodium hydride which was removed as before by extraction of an acetonitrile solution of the product with hexane. Evaporation of the acetonitrile gave the mixture of the methyl esters (20.5 g, 67.7%). Saponification of this mixture in methanolic potassium hydroxide (30 g, potassium hydroxide in 400 ml, 75% aqueous methanol) for 15 hrs gave after acidification a mixture of the acids which upon recrystallization from ethanol gave 5.81 g of a solid 45 (acid A) mp 224-227°; ir ($CHCl_3$) 3500-2500, 1700 cm^{-1}. Concentration of the mother liquor gave 8.65 of the acid 47 (B), mp 148-151° (lit.[51] 145-150°) which on recrystallization from ether gave colorless crystals: mp 153-155°; ir ($CHCl_3$) 1708 cm^{-1}; nmr ($CDCl_3$) τ 3.3 (m, 1H), 7.4 (t, J = 8 cps, 1H), 8.05 (dd, J_1 = 8 cps, J_2 = 5 cps, 1H), 8.7 (dd, J_1 = 5 cps, J_2 = 8 cps, 1H).

Reduction of 1,2-diphenylcyclopropylcarboxylic acid (A).

The acid (3.2 g) was dissolved in dry ether (150 ml) and added to a solution of lithium aluminum hydride (0.74 g) in 50 ml of ether. The mixture was refluxed with stirring for 12 hrs. After this time one ml of a saturated solution of sodium sulfate in water was added. The precipitated aluminum salts were then filtered and the clear ethereal solution washed with water and dried over magnesium sulfate. Evaporation of the ether yielded the solid alcohol 48 (A) (2.8 g, 93.8%) which was recrystallized from hexane to give feathery light crystals: mp 65-67.5°; ir ($CHCl_3$) 3650 cm^{-1} and 3500 cm^{-1} and 1050 cm^{-1}; nmr ($CDCl_3$) τ 3.05-3.25 (m, 10H), 6.5 (AB quartet, J = 12 cps, 2 m), 7.4 (broad singlets, 1H), 7.75 (dd, J_1 = 6 cps, J_2 = 8 cps, 1H), 8.6 (s, 1.5H), 8.72 (d, 1/2H, $\Delta\nu$ = 2 cps). The signal at 7.4 disappeared when the sample was treated with deuterium oxide.

<u>Anal</u>. Calcd. for $C_{16}H_{16}O$: C, 85.68; H, 7.19;

Found: C, 85.75; H, 7.31.

Preparation of 1,2-diphenylcyclopropylcarbinol (B) (49). Acid (B) (6 g) in dry ether (50 ml) was added to a suspension of lithium aluminum hydride (2 g) in dry ether (100 ml). The reaction was refluxed overnight. A saturated solution of sodium potassium tartrate was added (3.5 ml) and the mixture stirred for one half hour. The suspension was removed by filtration and the ether solution was washed with water, dried, and evaporated. An oily solid was obtained (4.4 g, 78.6%) which was crystallized from hexane to give cotton candy crystals (needles): mp 79-80°; ir ($CHCl_3$) 3600 cm^{-1}, 3450 cm^{-1}, 1050 cm^{-1}; nmr ($CDCl_3$) τ 2.7 (m, 10H), 6.7 (s, 2H), 7.58 (broad triplet, J = 7.5 cps, 1H), 8.6 (s, 1H), 8.68 (s, 1.5H), 8.76 (doublet, $\Delta\nu$ = 0.5 cps, 0.5H). The signal at 8.6 disappeared when the sample was shaken with deuterium oxide.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.68; H, 7.19;

Found: C, 85.63; H, 7.27.

Treatment of truxillic acid with lead tetraacetate. Truxillic acid (10 g, 0.033 mole) and lead tetraacetate (46.6 g, 0.1 mole) were suspended in dry benzene (250 ml) under a nitrogen atmosphere. Pyridine (15 ml) was added and the mixture was placed in a 70-80° oil bath. A light yellow clear solution was formed. After ten minutes the solution started to become turbid and a precipitate was formed. After 1.5 hrs ethyl acetate (50 ml) was added and the reaction mixture was filtered. The filtrate was treated with a solution of sodium *meta* bisulfite (200 ml of 3% solution). The white precipitate of lead oxide was filtered. The organic layer of the filtrate was separated and treated with sodium hydroxide solution (250 ml of a 5% solution) to remove the unreacted truxillic acid. The organic layer was dried and evaporated to give 8.6 g of a yellow oily solid. The solid was taken in ether—hexane (90:10) from which 4.8 g (57%) of a solid deposited 50; mp 173-174°; ir (Nujol) 1780 cm^{-1}; nmr ($CDCl_3$) 2.8 (s, 5H), 2.98 (m, 5H), 4.81 (dd, J_1 = 1.5 cps, J_2 = 7 cps, 1H), 5.76 (m, 1H), 5.92 (bs, 1H), 6.38 (dd, J_1 = 7 cps, J_2 = 3 cps, 1H); m/e 250.

<u>Anal</u>. Calcd. for $C_{17}H_{14}O_2$: C, 81.59; H, 5.65;
Found: C, 81.50; H, 5.96;

Addition of hexane to the filtrate caused deposition of a solid 51 (2.1 g, 24.8%) which was recrystallized from hexane-ether (50:50) to give needles: mp 132-133° (lit.[56,57] 133°); ir (Nujol) 1770 cm^{-1}; nmr ($CDCl_3$) τ 2.7 (bs, 10H), 5.26 (bs, 1H), 7.4 (m, 3H).

<u>Anal</u>. Calcd. For $C_{17}H_{14}O_2$: C, 81.59; H, 5.65;
Found: C, 81.75; H, 5.68.

Truxillic acid was treated with lead tetraacetate in acidic and neutral media. The following table summarizes the conditions and results of such experiments.

TABLE II

Treatment of Truxillic Acid with Lead Tetraacetate in Various Solvent Systems

RUN #	Truxillic acid, g	Lead Tetra-acetate, g	Recovered acid, g	Total Yield	Ratio 50/51	Time Hours	Solvent
1	8.88	71	3.7	32%	1.15/2.45	5	AcOH 300 ml
2	10	50	5.5	16%	2.5/1	5	Benzene 600 ml
3	10	60	7.5	0%	-	5	AcOH H_2O
4	5	32[a] recrystallized	9	45%	4/1	5	Benzene 400 ml
5	10	46	3.7	20%	1/2	10	130 ml AcOH 66 g Na_2CO_3

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[a] Lead tetraacetate recrystallized from acetic acid and dried in the dark.

Attempted isomerization of lactone 50 to lactone 51. Lactone 50 (500 mg) was taken in benzene (50 ml) and acetic acid (1 ml) was added and the solution was refluxed overnight. After 12 hrs the mixture was washed with water and sodium bicarbonate solution and dried. Evaporation of benzene yielded a solid (460 mg) which showed an nmr spectrum identical with that of starting material.

Treatment of α-phenylglutaric acid with lead tetraacetate. α-Phenylglutaric acid (7 g, 0.033 mole) was dissolved in benzene (150 ml) and lead tetraacetate (23.3 g, 0.05 mole) was added to the solution.

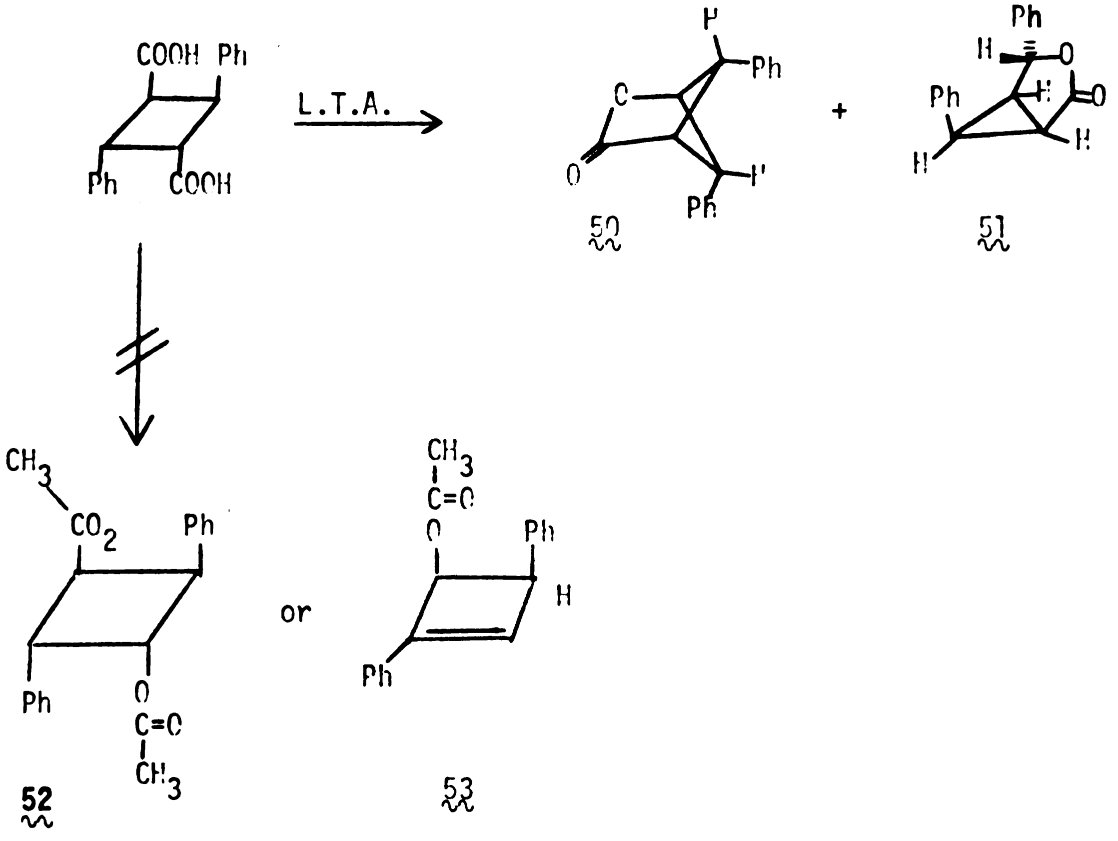
Pyridine (6 ml, 0.075 mole) was added and the mixture was heated in an oil bath to 75-80°. A yellow clear solution was formed which after a few minutes started to become cloudy and yielded a precipitate. Workup yielded 5.4 g (36%) of a yellow oil which was recrystallized from hexane to give 5.1 g of crystals, mp 34-36°, which had identical spectroscopic properties with γ-phenyl—γ-butyrolactone prepared before[47].

ANCILLARY SYNTHESIS

A DISCUSSION OF RESULTS

Reaction of lead tetraacetate with 1,3-dicarboxylic acids.

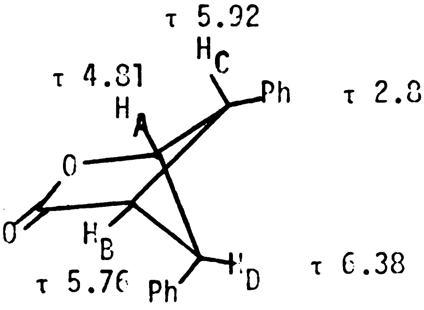
Lead tetraacetate has been used for oxidative decarboxylation of aliphatic carboxylic acids, and 1,2-diacids[58,59], to obtain the corresponding acetate or olefins. The earlier work suggested a direct oxidation to a carbonium ion intermediate, based on the isolated products[60]. Later work by Kochi[61,62,63], and Davis and Waring[64,65] showed that the primary product is a radical, although in certain cases, such as bicyclo[2.2.1]-hexane derivatives, the primary product is oxidized further to the corresponding carbonium ion and no product from a free radical intermediate is isolated[66,67]. In our studies of various methods for decarboxylation of α-truxillic acid **14**, we treated it with lead tetraacetate in the hope of converting it to a diacetate **52** or the cyclobutenyl acetate **53**. But the reaction instead yield lactones **50** and **51**.



50 **51** **52** **53**

When this reaction was carried out on glutaric acid and α-phenyl glutaric acid, the corresponding lactones were obtained in good yields. We therefore suggest that this could be a general reaction for conversion of 1,3-diacids to the corresponding γ-lactones.

Reaction of α-truxillic acid 14 with lead tetraacetate. The reaction was carried out in benzene solution in the presence of pyridine catalyst. The two products **51** and **52** were isolated by fractional crystallization. The product having mp 173-174°, gave an analysis consistent with $C_{17}H_{14}O_2$. The parent peak in the mass spectrum appeared at 250. It showed a very high frequency carbonyl absorption at 1816 cm^{-1} and the nmr spectrum exhibited a five proton singlet at τ 2.8, a five proton multiplet at τ 2.98, a one proton doublet of doublets at τ 4.81, J_1 = 1.5 cps, J_2 = 7 cps, a one proton multiplet at τ 5.76, a one proton broad singlet at τ 5.92, and a one proton doublet of doublets at τ 6.38, J_1 = 7 cps, J_2 = 3 cps. The ir spectrum is consistent with a β lactone or a very strained γ lactone. All possible β lactones are unacceptable based on the chemical shifts and coupling constants of the saturated protons and the expected reactions of cyclobutane-1,3-dicarboxylic acid **14**. The data are well explained, however, by structure **51**, which has an additionally strained γ-lactone in a bicyclo[2.1.1]system. The *trans* nature of the phenyls is consistent with the origin of the compound and required by the four different types of aliphatic protons, and two different types of phenyl protons in the nmr. The nmr peaks were assigned to various hydrogens as follows:

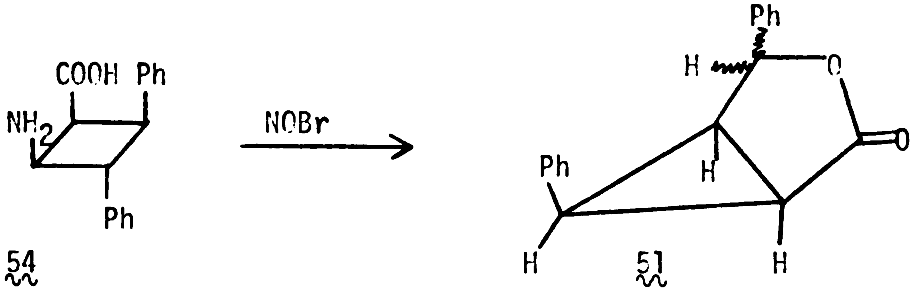


51

J_{AB} = 1 cps
J_{AD} = 7 cps
J_{BD} = 3 cps
J_{AC} and J_{BC} exist but are small.

The lowest field aliphatic signal at τ 4.81, was assigned to H_A, the bridgehead hydrogen alpha to the oxygen. The second low field signal at τ 5.76 was assigned to H_B, the bridgehead proton alpha to the carbonyl. Assignment of the other two signals to H_B and H_C was more difficult, because the magnetic anisotropic effect of the lactone bridge and the phenyls could not be determined with confidence. However, a decision could be made by consideration of coupling constants with reference to a molecular model. Thus, it was clear that H_A should be coupled more strongly to the proton anti to the lactone than to the syn proton. The anti proton must therefore be H_D (J_{AD} = 7 cps). The smaller coupling of H_B to H_D (3.cps) must reflect a distortion in the system which makes it unsymmetrical. This distortion might arise from the smaller C-O-C bond angle in the lactone or from steric repulsion of the syn phenyl, or both.

The other product of the reaction is reported in the literature. It was obtained by electrolytic oxidation of truxillic acid[57], and also by nitrosyl bromide deamination of γ-truxinic amino acid 54[56].



54

51

The ir spectrum (-C=O at 1770 cm^{-1}) is in accordance with the 5-membered ring lactone. Our work provides no further stereochemical evidence for the suggested <u>syn</u> structure. The one proton singlet at τ 5.26 was assigned to the proton α to the oxygen and the three proton multiplet at 7.4 was assigned to the cyclopropane hydrogens.

When the reaction of α-truxillic acid was carried out in different solvent systems, it appeared that the ratio of 50/51 was related to the acidity or basicity of the solvent system. When the lead tetraacetate was freed from acetic acid, the ratio of 51/50 was found to be 4/1 while in acetic acid the ratio was 1/2.5. In order to find out whether acetic acid is responsible for rearrangement of 50 to 51, lactone 50 was refluxed in benzene in the presence of acetic acid. The starting material was recovered after 24 hrs almost quantitatively and lactone 51 could not be detected in the product. Formation of lactone 50 from α-truxillic acid gives a novel and unique method for preparation of bicyclic[2.1.1]lactones. To our knowledge this is the first example of such a class of lactone to have been prepared.

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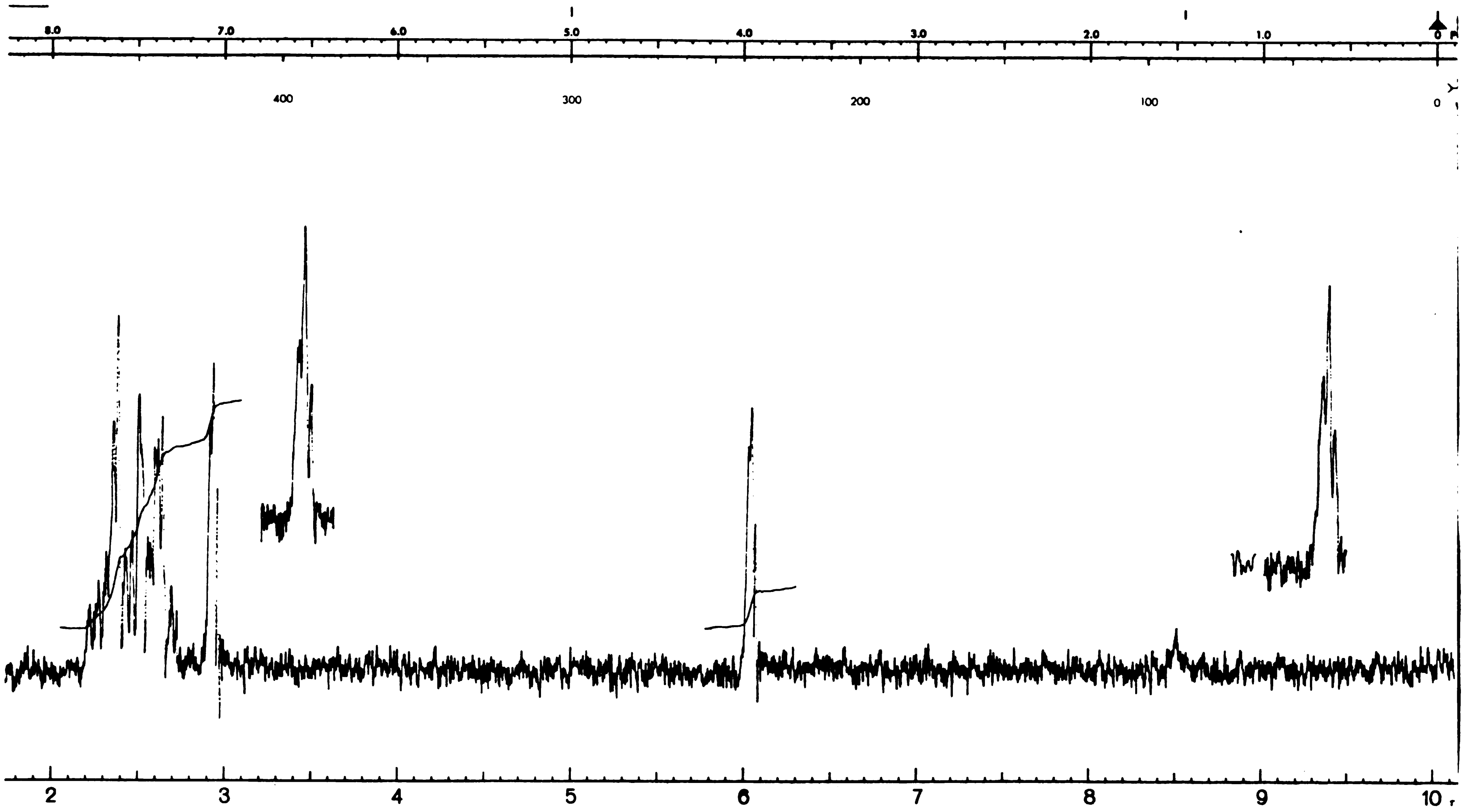

FIGURE 1

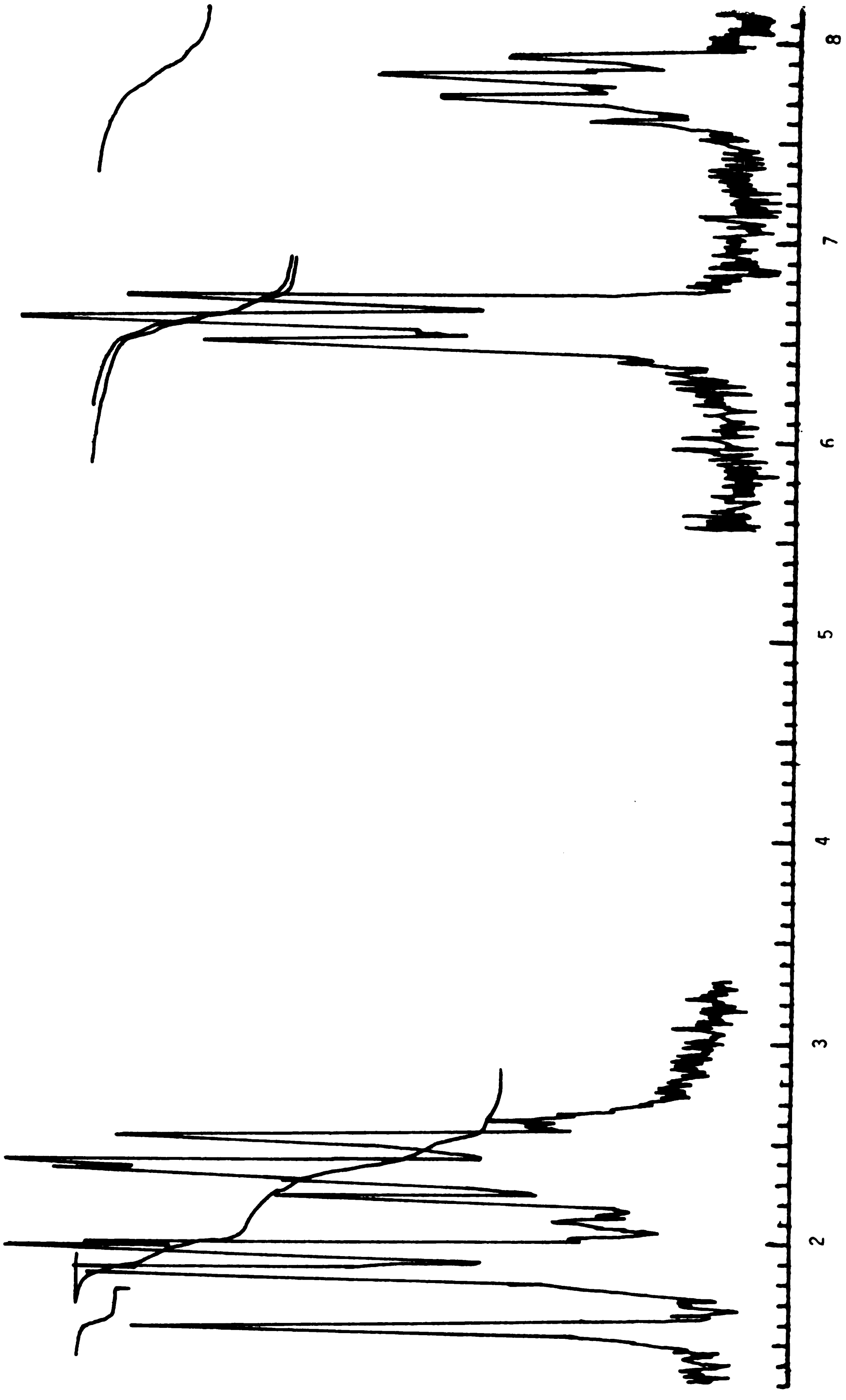

FIGURE 2

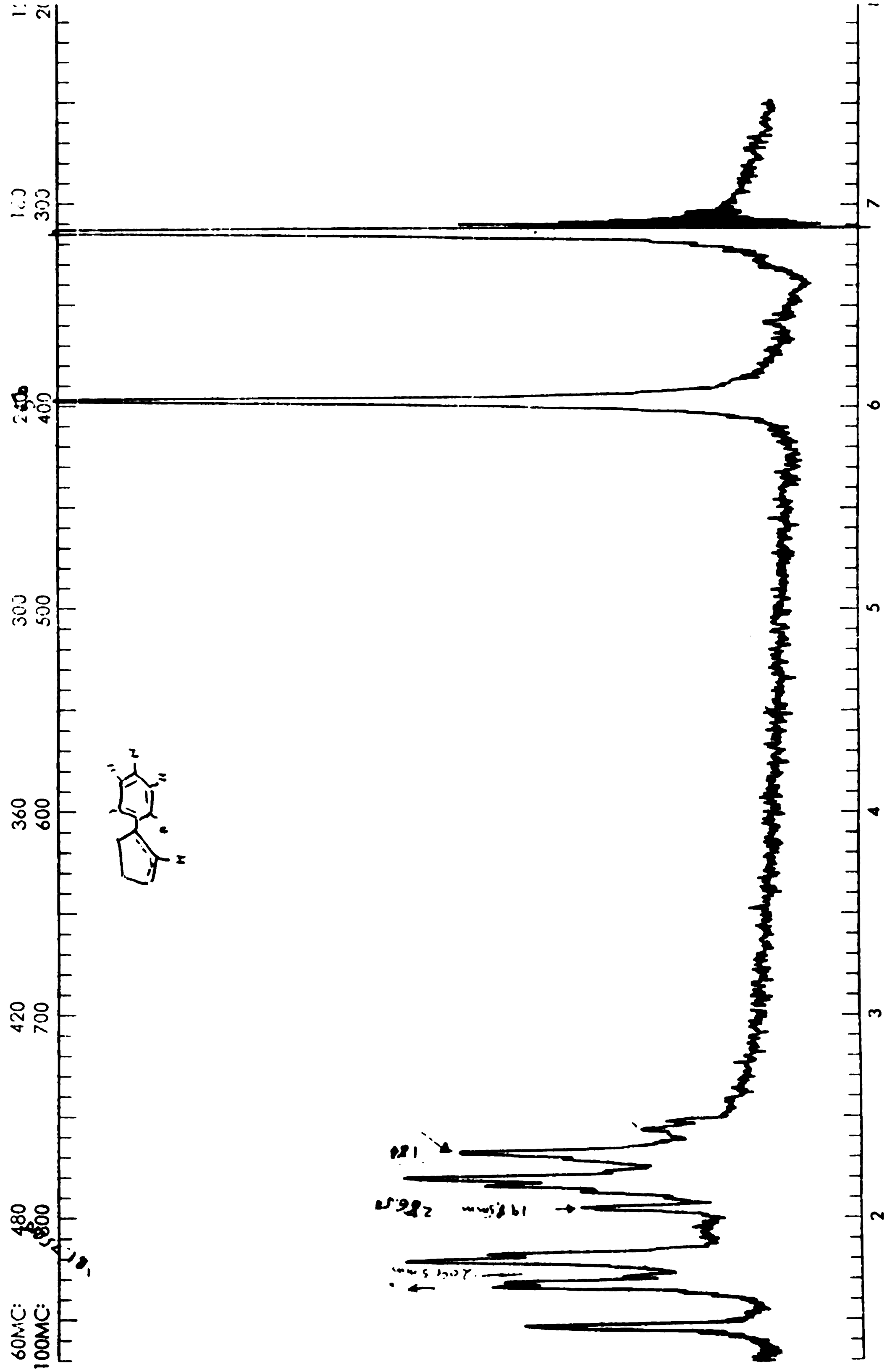
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FIGURE 3

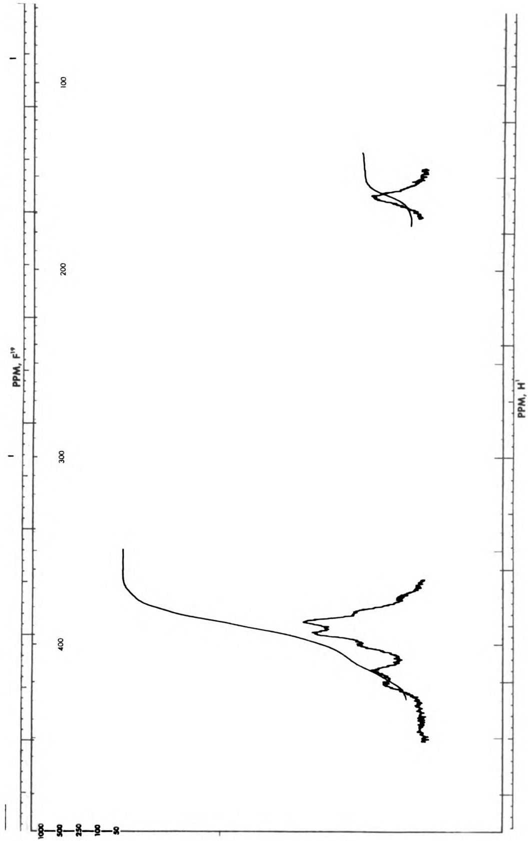

FIGURE 4

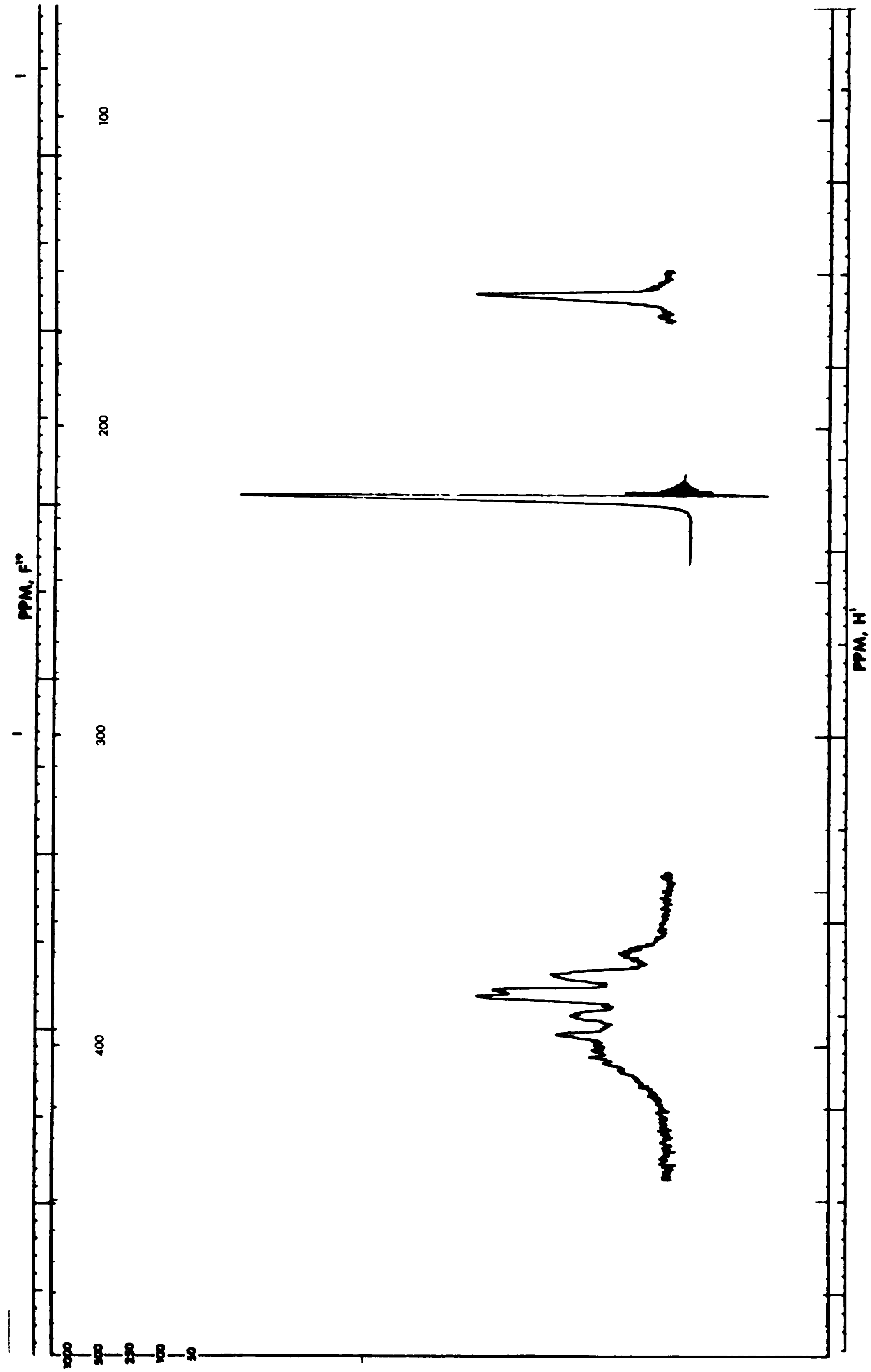

FIGURE 5

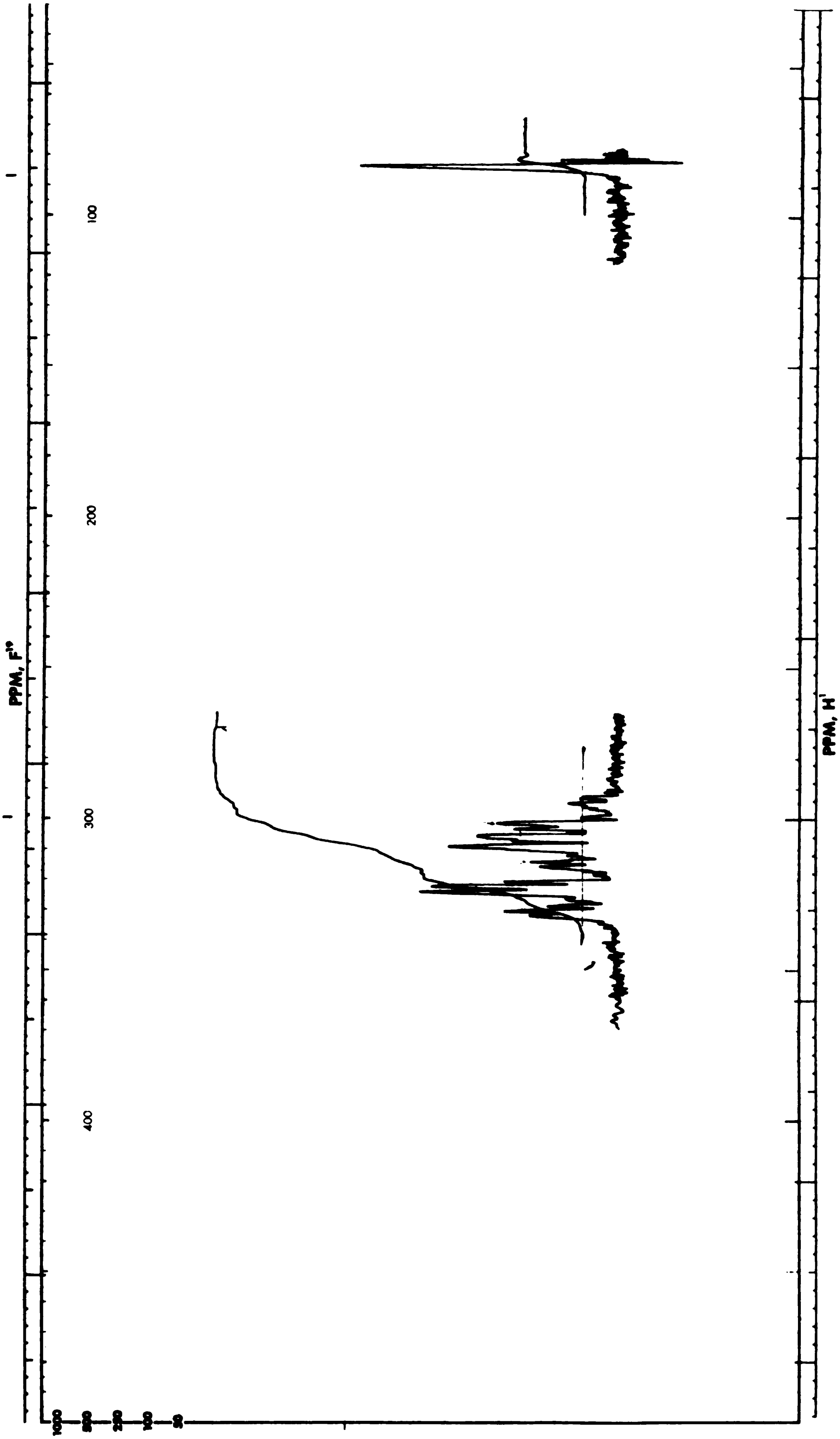

FIGURE 6

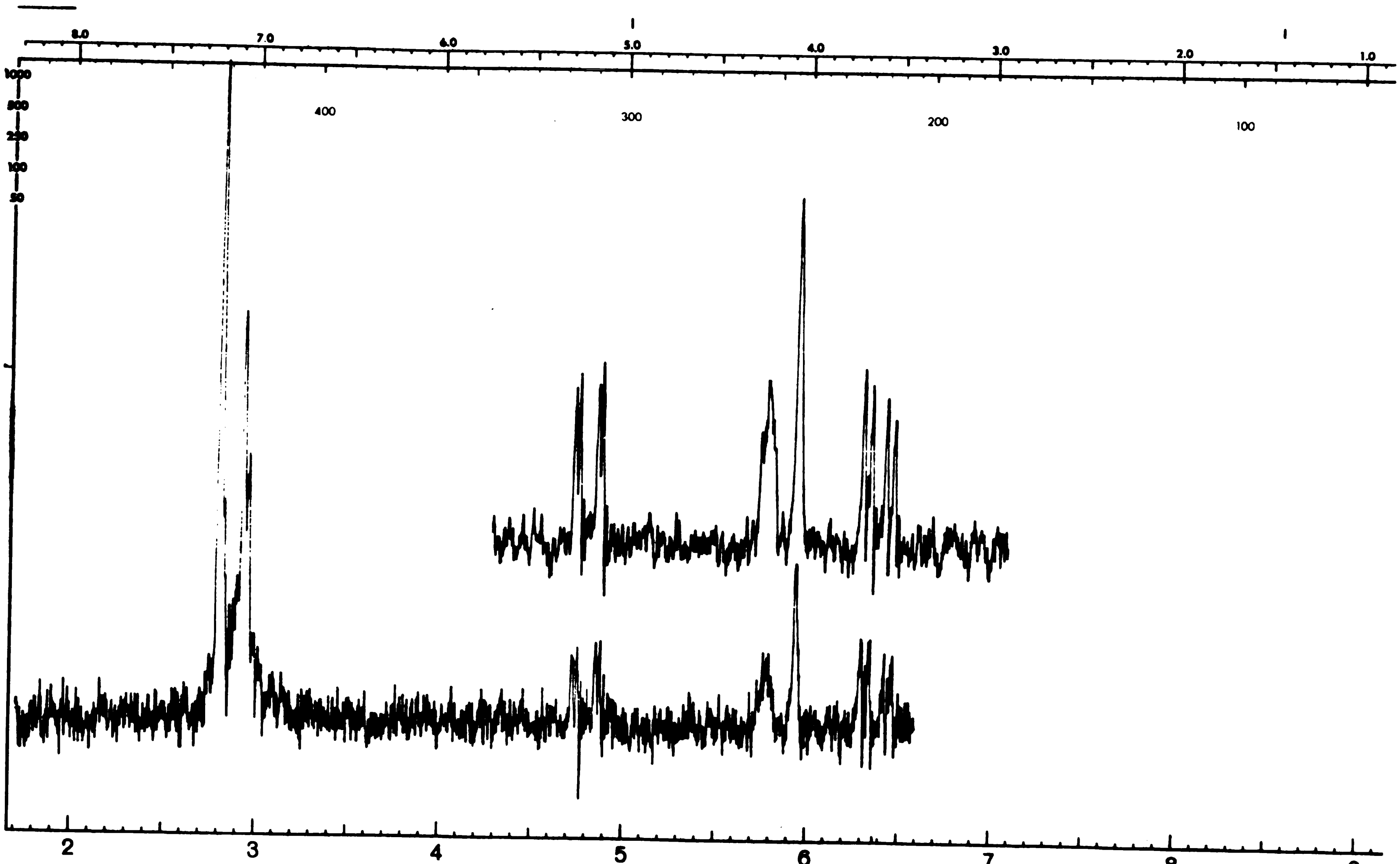
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FIGURE 7